Access DB# 94/77

SEARCH REQUEST FORM

Scientific and Technical Information Center

Lequester's Full Name: LEFF PAIZICE Examiner #: 72607 Date: 05/03 art Unit: 1648 Phone Number 30 8 - 2227 Serial Number: 09/623 533 Mail Box and Bldg/Room Location: 040/ Results Format Preferred (circle): PAPER DISK E-MAIL 86/5										
Please provide a detailed statement of the s Include the elected species or structures, ke	search topic, and describe eywords, synonyms, acror that may have a special me	as specifically as possible the subject matter to be searched. syms, and registry numbers, and combine with the concept or eaning. Give examples or relevant citations, authors, etc, if								
Title of Invention:										
Inventors (please provide full names):										
Earliest Priority Filing Date:										
For Sequence Searches Only Please includ appropriate serial number.	le all pertinent information (parent, child, divisional, or issued patent numbers) along with the								
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Online Time:	Other	Other (specify)								

PTO-1590 (8-01)

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FILE COVERS 1907 - 20 May 2003 VOL 138 ISS 21 FILE LAST UPDATED: 19 May 2003 (20030519/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES: RING(S) ARE ISOLATED OR EMBEDDED NUMBER OF NODES IS 21

STEREO ATTRIBUTES: NONE

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ANSWER 1 OF 21 HCAPLUS COPYRIGHT 2003 ACS 2002:660233 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER:

137:365153

TITLE: Kinetics of tethering quaternary ammonium compounds to

K+ channels

AUTHOR(S): Blaustein, Robert O.

Department of Biochemistry, Brandeis University, CORPORATE SOURCE:

Waltham, MA, 02454, USA

Journal of General Physiology (2002), 120(2), 203-216 SOURCE:

CODEN: JGPLAD; ISSN: 0022-1295 Rockefeller University Press

PUBLISHER: DOCUMENT TYPE: Journal LANGUAGE: English

Polymeric maleimido-quaternary ammonium (QA) compds. have been shown to function as mol. tape measures when covalently tethered to external cysteine residues of a Shaker K+ channel (Blaustein R.O., P.A. Cole, C. Williams, and C. Miller. 2000. Nat. Struct. Biol. 7:309-311). sufficiently long compds., the cysteine-maleimide tethering reaction creates a high concn., at the channel's pore, of a TEA-like moiety that irreversibly blocks current. This paper investigates a striking feature of the maleimide-cysteine tethering kinetics. Strong blockers-those that induce substantial levels (>80%) of irreversible inhibition of current-react with channel cysteines much more rapidly than weak blockers and, when delivered to channels with four cysteine targets, react with multiexponential kinetics. This behavior is shown to arise from the ability of a strong blocker to conc. its maleimide end near a channel's cysteine target by exploiting the reversible pore-blocking affinity of its OA headgroup.

475558-09-9 475558-10-2 ΙT

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(difference in behavior between these two blockers of potassium channels result from ability of strong blokes to acts as affinity label)

THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: 41 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 2 OF 21 HCAPLUS COPYRIGHT 2003 ACS 2002:615671 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER:

137:164122

TITLE:

Long lasting growth hormone releasing factor

derivatives

INVENTOR(S):

Bridon, Dominique P.; Boudjellab, Nissab; Leger, Roger; Robitaille, Martin; Jette, Lucie; Benquet,

Corinne

PATENT ASSIGNEE(S):

Conjuchem Inc., Can. PCT Int. Appl., 65 pp.

SOURCE: CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	TENT	NO.		KI	ND [DATE			A	PPLI	CATI	и ис	ο.	DATE			
WO	2002	0628	4 4	A.	2 .:	20020	0815		W	20°	02-C	A123		20020	0201		
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		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FΙ,	GB,	GD,	GE,	GH,
														ΚZ,			
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		PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TN,	TR,	TT,	ΤZ,

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UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
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                             20030417
                                             US 2002-203809
                                                             20020812
     US 2003073630
                        Α1
PRIORITY APPLN. INFO.:
                                          US 2001-266424P P
                                                               20010202
                                          WO 2002-CA123
                                                               20020201
                          MARPAT 137:164122
OTHER SOURCE(S):
     This invention relates to growth hormone releasing factor (GRF) derivs.
     In particular, this invention relates to GRF peptide derivs. having an
     extended in vivo half-life, for promoting the endogenous prodn. or release
     of growth hormone in humans and animals. The deriv. comprises a GRF
     peptide or analog comprising a reactive entity coupled thereto and capable
     of reacting with available functionalities on a blood component to form a
     stable covalent bond. The reactive entity may be coupled to the
     N-terminal of the peptide, the C-terminal of the peptide, or to an other
     available site along the peptidic chain. Pharmaceutical compns. contg.
     the GRF derivs. and therapeutic uses of the GRF derivs. are also claimed.
ΙT
     446037-12-3P 446037-14-5P
     RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic
     preparation); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (prepn. and use of long lasting growth hormone releasing factor
        derivs.)
     ANSWER 3 OF 21 HCAPLUS COPYRIGHT 2003 ACS
                          2001:430337 HCAPLUS
ACCESSION NUMBER:
                          135:211262
DOCUMENT NUMBER:
                          Design, synthesis and properties of synthetic
TITLE:
                          chlorophyll proteins
                          Rau, Harald K.; Snigula, Heike; Struck, Andreas;
AUTHOR(S):
                          Robert, Bruno; Scheer, Hugo; Haehnel, Wolfgang
                          Institut fur Biologie II/Biochemie,
CORPORATE SOURCE:
                          Albert-Ludwigs-Universitat Freiburg, Freiburg,
                          D-79104, Germany
                          European Journal of Biochemistry (2001), 268(11),
SOURCE:
                          3284-3295
                          CODEN: EJBCAI; ISSN: 0014-2956
                          Blackwell Science Ltd.
PUBLISHER:
DOCUMENT TYPE:
                          Journal
LANGUAGE:
                          English
     A chemoselective method is described for coupling chlorophyll derivs. with
   an aldehyde group to synthetic peptides or proteins modified with an
     aminoxyacetyl group at the .epsilon.-amino group of a lysine residue.
     Three template-assembled antiparallel four-helix bundles were synthesized
     for the ligation of one or two chlorophylls. This was achieved by
     coupling unprotected peptides to cysteine residues of a cyclic decapeptide
     by thioether formation. The amphiphilic helixes were designed to form a
     hydrophobic pocket for the chlorophyll derivs. Chlorophyll derivs.
     Zn-methyl-pheophorbide b and Zn-methyl-pyropheophorbide d were used.
     aldehyde group of these chlorophyll derivs. was ligated to the modified
     lysine group to form an oxime bond. The peptide-chlorophyll conjugates
     were characterized by electrospray mass spectrometry, anal. HPLC, and
     UV/visible spectroscopy. Two four-helix bundle chlorophyll conjugates
     were further characterized by size-exclusion chromatog., CD, and resonance
     Raman spectroscopy.
ΙT
     216884-15-0P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
```

THERE ARE 78 CITED REFERENCES AVAILABLE FOR THIS

(prepn. and properties of synthetic chlorophyll proteins using template-assembled antiparallel amphiphilic four-helix bundles)

78

REFERENCE COUNT:

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 4 OF 21 HCAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 2001:185609 HCAPLUS

DOCUMENT NUMBER: 134:237836

TITLE: Preparation of peptides for pulmonary delivery

compositions via bioconjugation

INVENTOR(S): Ezrin, Alan M.; Fleser, Angelica; Robitaille, Martin;

Milner, Peter G.; Bridon, Dominique P.

PATENT ASSIGNEE(S): SOURCE:

Conjuchem, Inc., Can. PCT Int. Appl., 184 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PATENT NO. KIND			DATE	DATE APPLICATION NO. DATE													
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			CF,	CG,	CI,	CM,	GA,	GN,	GW,	ML,	MR,	NE,	SN,	TD,	TG			
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				_						WO 2	000-	IB14	29	W	2000	0907		

AB Methods and compns. for pulmonary delivery of therapeutic agents which are capable of forming covalent bonds with a site of interest or which have formed a covalent bond with a pulmonary soln. protein are disclosed. A modified therapeutic agent comprises a therapeutic agent (GP-41 peptides, BBB peptides, anticancer agents, antihistamines, etc.) and a reactive group which reacts in vivo with amino, hydroxyl or thiol groups on pulmonary components or blood components to form a stable covalent bond. In the examples, a series of peptides (e.g., modified RGD peptide AGYKPEGKRGDAK) were synthesized by the solid phase method.

IT 307314-62-1P 329716-72-5P 329716-74-7P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of peptides for pulmonary delivery compns. for bioconjugation)

ANSWER 5 OF 21 HCAPLUS COPYRIGHT 2003 ACS 2000:824301 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER:

134:13338

TITLE:

Long lasting insulinotropic peptides

INVENTOR(S):

Bridon, Dominique P.; L'Archeveque, Benoit; Ezrin, Alan M.; Holmes, Darren L.; Leblanc, Anouk; St.

Pierre, Serge

PATENT ASSIGNEE(S): SOURCE:

Conjuchem, Inc., Can. PCT Int. Appl., 96 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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       WO 2000069911
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
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PRIORITY APPLN. INFO.:
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                                                          WO 2000-IB763
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                                                          WO 2000-US13563 W 20000517
                                                          US 2000-623618
                                                                                   A3 20000905
       Modified insulinotropic peptides are disclosed. The modified
AΒ
       insulinotropic peptides are capable of forming a peptidase stabilized
       insulinotropic peptide. The modified insulinotropic peptides are capable
       of forming covalent bonds with one or more blood components to form a
       conjugate. The conjugates may be formed in vivo or ex vivo. The modified
       peptides are administered to treat humans with diabetes and other related
       diseases.
IΤ
       307315-09-9P
       RL: SPN (Synthetic preparation); PREP (Preparation)
            (long lasting insulinotropic peptides with antidiabetic activity)
                                             THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
REFERENCE COUNT:
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                                             RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
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Page 5.

ANSWER 6 OF 21 HCAPLUS COPYRIGHT 2003 ACS

2000:824291 HCAPLUS

ACCESSION NUMBER:

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DOCUMENT NUMBER:
                          134:21425
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TITLE: Protection of endogenous therapeutic peptides from

peptidase activity through conjugation to blood

components

INVENTOR(S): Bridon, Dominique P.; Ezrin, Alan M.; Milner, Peter

G.; Holmes, Darren L.; Thibaudeau, Karen

PATENT ASSIGNEE(S): SOURCE:

Conjuchem, Inc., Can. PCT Int. Appl., 733 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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PRIORITY APPLN. INFO.:
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                                                                       US 1999-159783P P · 19991015
                                                                       EP 2000-932570
                                                                                                    A3 20000517
                                                                       WO 2000-IB763
                                                                                                     W 20000517
                                                                       WO 2000-US13576 W 20000517
        A method for protecting a peptide from peptidase activity in vivo, the
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AB peptide being composed of between 2 and 50 amino acids and having a C-terminus and an N-terminus and a C-terminus amino acid and an N-terminus amino acid is described. In the first step of the method, the peptide is modified by attaching a reactive group to the C-terminus amino acid, to the N-terminus amino acid, or to an amino acid located between the

Parkin 09_623533

N-terminus and the C-terminus, such that the modified peptide is capable of forming a covalent bond in vivo with a reactive functionality on a blood component. The solid phase peptide synthesis of a no. of derivs. with 3-maleimidopropionic acid (3-MPA) is described. In the next step, a covalent bond is formed between the reactive group and a reactive functionality on a blood component to form a peptide-blood component conjugate, thereby protecting said peptide from peptidase activity. The final step of the method involves the analyzing of the stability of the peptide-blood component conjugate to assess the protection of the peptide from peptidase activity. Thus, the percentage of a K5 kringle peptide (Pro-Arg-Lys-Leu-Tyr-Asp-Lys-NH2) conjugated to human serum albumin via MPA remained relatively const. through a 24-h plasma, assay in contrast to unmodified K5 which decreased to 9% of the original amt. of K5 in only 4 h

224785-55-1P 224785-62-0P 307314-59-6P ΙT 307314-61-0P 307314-63-2P 307314-65-4P 307314-67-6P 307314-69-8P 307314-71-2P 307314-73-4P 307314-78-9P 307314-79-0P 307314-80-3P 307315-09-9P 307315-10-2P 307315-11-3P 307315-16-8P

RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);

(protection of endogenous therapeutic peptides from peptidase activity through conjugation to blood components)

ANSWER 7 OF 21 HCAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 2000:425768 HCAPLUS

DOCUMENT NUMBER:

TITLE:

133:144752

AUTHOR(S):

Site specific 1:1 opioid:albumin conjugate with in vitro activity and long in vivo duration

Holmes, Darren L.; Thibaudeau, Karen; L'Archeveque, Benoit; Milner, Peter G.; Ezrin, Alan M.; Bridon,

CORPORATE SOURCE: SOURCE:

ConjuChem Inc., Montreal, QC, H2X 3Y8, Can. Bioconjugate Chemistry (2000), 11(4), 439-444

CODEN: BCCHES; ISSN: 1043-1802

American Chemical Society

PUBLISHER: DOCUMENT TYPE:

Journal

LANGUAGE: English

A site-specific 1:1 dynorphin A-(1-13)-NH2 deriv. conjugated specifically to Cys 34 on human serum albumin (CCI-1035) was shown to be an opioid receptor agonist in vitro and to be a long lasting antinociceptive agent when administered i.v. to mice as assessed by an acetic acid writhing assay. When 10 .mu.mol/kg of CCI-1035 was administered to mice, rapid antinociception was obsd. within 5 min following i.v. bolus injection and was sustained beyond 8 h. Antinociceptive activity was absent in a heat induced pain model using a mouse tail-flick assay. This finding represents the first report of a 1:1 albumin opioid conjugate retaining potent in vivo activity equal to or greater than dynorphin A, accompanied by a dramatic extension in duration of action. This novel site-specific bioconjugation technol. produces an agent that may be useful for 287726-97-0

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(albumin conjugate; site specific 1:1 opioid:albumin conjugate with in vitro activity and long in vivo duration) 37

REFERENCE COUNT:

THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4ANSWER 8 OF 21 HCAPLUS COPYRIGHT 2003 ACS

Parkin 09 623533

ACCESSION NUMBER: 2000:283519 HCAPLUS

133:319675 DOCUMENT NUMBER:

Synthetic four-helix-bundle protein carrying 1 or 2 TITLE:

chlorophyll derivatives

Struck, A.; Snigula, H.; Rau, H.-K.; Horth, P.; AUTHOR(S):

Scheer, H.; Haehnel, W.

Biologie II, University of Freiburg, Freiburg, CORPORATE SOURCE:

D-79104, Germany

Photosynthesis: Mechanisms and Effects, Proceedings of SOURCE:

the International Congress on Photosynthesis, 11th,

Budapest, Aug. 17-22, 1998 (1998), Volume 5,

4213-4216. Editor(s): Garab, Gyozo. Kluwer Academic Publishers: Dordrecht, Neth.

CODEN: 68VVAS

DOCUMENT TYPE: LANGUAGE:

Conference English

The structures of several (bacterio) chlorophyll proteins have elucidated AΒ on the interactions between proteins and cofactors. A study was conducted whereby synthetic proteins were designed with similar cofactors. Based on recent success in designing heme proteins, a modular strategy was taken, which relies on a synthesis of a four helix bundle. In order to reduce potential complications, three structural modifications were introduced in the current work. The synthetic peptides were loaded with 1 or 2 chlorophyll a derivs. such that they were principally capable of an edge-to-edge interaction, reminiscent of the B850, B870 pigments in LH2, LH1 and RC, resp., from purple bacteria.

303013-27-6P ΙT

RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(amino acid sequence; synthetic four-helix-bundle protein carrying 1 or

2 chlorophyll derivs.) REFERENCE COUNT:

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 9 OF 21 HCAPLUS COPYRIGHT 2003 ACS 2000:240433 HCAPLUS ACCESSION NUMBER:

133:27800 DOCUMENT NUMBER:

Tethered blockers as molecular "tape measures" for a TITLE:

voltage-gated K+ channel

Blaustein, Robert O.; Cole, Philip A.; Williams, AUTHOR(S):

Carole; Miller, Christopher

Department of Biochemistry, Howard Hughes Medical CORPORATE SOURCE:

Institute, Brandeis University, Waltham, MA, 02454,

USA

Nature Structural Biology (2000), 7(4), 309-311 SOURCE:

CODEN: NSBIEW; ISSN: 1072-8368

Nature America PUBLISHER:

DOCUMENT TYPE: Journal English LANGUAGE:

The propagation of elec. signals in excitable cells is orchestrated by a mol. family of voltage-dependent ion channel proteins. These K+, Na+, and Ca++ channels are all composed of four identical or similar units, each contg. six transmembrane segments (S1-S6) in a roughly four-fold sym. structure. The S5-S6 sequences fold into a central pore unit, which is surrounded by a voltage-gating module composed of S1-S4. The recent structure of KcsA, a two-transmembrane bacterial K+ channel, illuminates the phys. character of the pore unit, but little is known about the arrangement of the surrounding S1-S4 sequences. To locate regions of this gating module in space, we synthesized a series of compds. of varying length that function as mol. "tape measures": quaternary ammonium (QA) pore blockers that can be tethered to specific test residues. We show that in a Shaker K+ channel, the extracellular ends of S1 and S3 are .apprx.30 .ANG. from the tetraethylammonium (TEA) blocking site at the

```
external opening of the pore. A portion of the S3-S4 loop is, at 17-18
     .ANG., considerably closer.
     274258-94-5 274258-95-6 274258-97-8
IT
     274258-99-0 274259-00-6 274259-01-7
     RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
     (Uses)
        (quaternary ammonium pore blockers show extracellular ends of S1 and S3
        transmembrane segments of Shaker K+ channel are .apprx.30.ANG. from TEA
       blocking site at pore opening)
                         22
                               THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS
REFERENCE COUNT:
```

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 10 OF 21 HCAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 1999:795852 HCAPLUS

DOCUMENT NUMBER:

132:34768

TITLE:

Divalent antibody fragments

INVENTOR(S):

Chapman, Andrew Paul; King, David John

PATENT ASSIGNEE(S):

Celltech Therapeutics Limited, UK

SOURCE:

PCT Int. Appl., 43 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

```
KIND DATE
      PATENT NO.
                                                       APPLICATION NO. DATE
                            Al 19991216
                                                       WO 1999-GB1800 19990608
      WO 9964460
           W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,
                MD, RU, TJ, TM
           RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
                 ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
                 CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                           AA 19991216
      CA 2330186
                                                     CA 1999-2330186 19990608
                                    19991230
                                                       AU 1999-42783
                                                                              19990608
      AU 9942783
                             Α1
                                                    GB 2000-30176
FD 1000
      GB 2354242
                                    20010321
                                                                              19990608
                             Α1
                                                       EP 1999-955481
      EP 1090037
                            A1
                                    20010411
                                                                              19990608
               AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
                IE, FI
                           . . .
                                    20010628
                                                        DE 1999-19983347 19990608
      DE 19983347
                             T
                                                        JP 2000-553466 19990608
1998-12545 A 19980610
      JP 2002517515
                             T2
                                    20020618
PRIORITY APPLN. INFO.:
                                                    GB 1998-12545
                                                    WO 1999-GB1800
                                                                        W 19990608
```

Divalent antibody fragments are described, each of which has one or more AΒ interchain bridges contg. a synthetic or naturally occurring polymer selected from a polyalkylene, polyalkenylene, polyoxyalkylene or polysaccharide. Each bridge may be the residue of a homo- or heterobifunctional crosslinking reagent and serves to link two heavy chains in each antibody fragment via the sulfur atoms of cysteine residues present in the chains. Each fragment may be attached to one or more effector or reporter mols., and is of use in therapy or diagnostics where it has markedly improved binding and/or pharmacokinetic properties when compared to other antibody fragments which have the same no. and type of polymer mols. but in which the polymer mols. are randomly attached. antibody fragment is selective to cell surface antigen, e.g. human TNF.alpha., PDGF, or a receptor thereof.

252335-95-8P 252335-97-0P ΙT

RL: BUU (Biological use, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation);

INVENTOR(S): Ezrin, Alan M.; Bridon, Dominique P.; Holmes, Darren L.; Milner, Peter

PATENT ASSIGNEE(S): Conjuchem, Inc., Can. SOURCE: PCT Int. Appl., 35 pp.

CODEN: PIXXD2

DOCUMENT TYPE: LANGUAGE: Patent English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

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PATENT NO.
                         KIND DATE · APPLICATION NO. DATE
                         A2
      WO 9924074
                                 19990520
                                                  WO 1998-US23704 19981106
                                19990819
      WO 9924074
                         А3
          W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
          DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, CA, CN, CH, ML, MB, NE, SN, TD, TC
               CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                        AA 19990520 CA 1998-2301799 19981106
      CA 2301799
     AU 9913127
                          A1
                                 19990531
                                                  AU 1999-13127
                                                                       19981106
     AU 750387
                                 20020718
                         B2
                                 20000614
                                                  EP 1998-956656
     EP 1007561
                         A2
                                                                       19981106
     EP 1007561
                         В1
                                 20020417
             AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
               IE, SI, LT, LV, FI, RO
      JP 2001522817
                        Т2
                                                                       19981106
                                 20011120
                                                  JP 2000-520159
                                 20020102
                                                  EP 2001-121557
                                                                      19981106
     EP 1167383
                          Α1
                               20030326
     EP 1167383
                         B1
          R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
               IE, SI, LT, LV, FI, RO
     EP 1199566
                          A1 20020424
                                                  EP 2001-126379 19981106
              AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
               IE, SI, LT, LV, FI, RO, MK, CY, AL
                                                   AT 1998-956656
     AT 216402
                                 20020515
                                                                       19981106
                          Ε
                                                   ES 1998-956656
                           Т3
     ES 2173641
                                 20021016
                                                                      19981106
                                                   AT 2001-121557
     AT 235513
                          Ε
                                 20030415
                                                                      19981106
                                                  US 1999-445986
     US 6437092
                          В1
                                 20020820
                                                                      19991216
     US 2001018420
                         A1
                                 20010830
                                                   US 2001-798119
                                                                       20010301
     US 2001018421
                          A1
                                 20010830
                                                   US 2001-798121
                                                                       20010301
     US 6500918
                           B2
                                 20021231
                                                  US 2001-798114
                                                                     20010301
     US 2002039999
                        A1
                                 20020404
                                               US 1997-64705P P 19971107
PRIORITY APPLN. INFO.:
                                                                  P 19980313
                                               US 1998-77927P
                                               EP 1998-956656
                                                                  A3 19981106
                                               EP 1998-959387
                                                                   A3 19981106
                                               WO 1998-US23704 W 19981106
                                               US 1999-445986 A3 19991216
```

AB Conjugates are prepd. from antinociceptive agents, particularly opioids or

opioid analogs, more particularly dynorphins, endorphins, deltorphins, enkephalins or analogs thereof, by combining said antinociceptive agent with a material providing a functionally reactive group capable of reacting with a blood component (preferably a blood cell or protein). Said conjugates permit extension of the therapeutic life of the antinociceptive agent. They may be administered to patients to alleviate pain, produce analgesic effects, or assist in cases of narcotics withdrawal, and may also be used as probes for receptor activity. administration to the patient may be made either in vivo or ex vivo and may be performed by either introducing the deriv. including the reactive functional group into the patient's vascular system or prepg. such a conjugate externally (or in vitro) and introducing that conjugate to the patient's vascular system.

224785-55-1P 224785-62-0P ΙT

> RL: PNU (Preparation, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(conjugates of opioids and endogenous carriers for extension of therapeutic life of analgesics)

ANSWER 12 OF 21 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1998:649172 HCAPLUS

DOCUMENT NUMBER:

130:66795

TITLE:

Modular synthesis of de novo-designed metalloproteins

for light-induced electron transfer

AUTHOR(S):

Rau, Harald K.; DeJonge, Niels; Haehnel, Wolfgang

CORPORATE SOURCE:

Institut fur Biologie II/Biochemie,

Albert-Ludwigs-Universitat Freiburg, Freiburg,

D-79104, Germany

SOURCE:

Proceedings of the National Academy of Sciences of the

United States of America (1998), 95(20), 11526-11531

CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER:

National Academy of Sciences

DOCUMENT TYPE: LANGUAGE:

Journal English

The design and chem. synthesis of two de novo four-helix bundle proteins is described; each protein has two bound cofactors. Their construction from purified peptides is based on the modular assembly of different amphiphilic helixes by chemoselective coupling to a cyclic peptide template. In the hydrophobic interior of the antiparallel four-helix bundle these proteins contain a heme in a binding pocket with two ligating His residues. A ruthenium tris(bipyridine) complex is covalently bound to different positions at the hydrophilic side of one of the heme-binding

helixes. Laser-induced electron transfer across the varied distance through this helix has been studied and compared with a pathway anal. UV-visible, CD, and mass spectra are consistent with the structure and orientation predetd. by the template.

ΙT 216884-15-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(modular synthesis of de novo-designed metalloproteins for `

light-induced electron transfer)

REFERENCE COUNT:

36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 13 OF 21 HCAPLUS COPYRIGHT 2003 ACS 1997:385683 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER:

127:5355

TITLE: Preparation of GnRH/reduced Pseudomonas exotoxin conjugates as sterilizing and anticancer agents

INVENTOR(S): Tolman, Richard L.; Lombardo, Victoria K. Merck and Co., Inc., USA; Tolman, Richard L.; PATENT ASSIGNEE(S):

Lombardo, Victoria K.

SOURCE:

PCT Int. Appl., 46 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PA	FENT	NO.		KI	ND	DATE			. A.	PPLI	CATI	ON NO	0.	DATE				
	WO	9715	317		Α	1	1997	0501		W	0 19	96-U	s170	 41	1996	1023			
		W:	AL,	AM,	ΑU,	AZ,	BA,	BB,	BG,	BR,	BY,	CA,	CN,	CU,	CZ,	EE,	GE,	HU,	
			IL,	IS,	JP,	KG,	KR,	ΚZ,	LC,	LK,	LR,	LT,	LV,	MD,	MG,	MK,	MN,	MX,	
			NO,	ΝZ,	PL,	RO,	RU,	SG,	SI,	SK,	ТJ,	TM,	TR,	TT,	UA,	US,	UZ,	VN,	
			AM,	ΑZ,	BY,	KG,	ΚZ,	MD,	RU,	ТJ,	TM								
		RW:	KΕ,	LS,	MW,	SD,	SZ,	UG,	ΑT,	ΒĖ,	CH,	DE,	DK,	ES,	FI,	FR,	GB,	GR,	
			ΙE,	ΙΤ,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	ML,	
			MR,	ΝE,	SN,	TD,	TG								•				
	ΑU	9674	717		A	1	1997	0515		Α	J 19	967	4717		1996	1023			
	EP	8596	24		A	1	1998	0826		E	P 19	96-9	3692	1	1996	1023			
		R:	ΑT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙΤ,	LI,	LU,	NL,	SE,	PT,	ΙE,	ΓI
	JP	1151	4380		T	2	1999	1207		J1	P 19	96-5	1676	9	1996	1023			
PRI	ORIT	APP	LN.	INFO	.:				1	US 19	995-	5899:	P	P	1995	1027			
									Ī	WO 19	996-1	US17	041	W	19963	1023			
OTH	IER SO	DURCE	(S):			MAR	PAT	127:	5355										

Ι

GI

Q-Ser-Tyr-NCHCO-X¹-Arg-Y-Z
$$(CH_2)_p-B-(CH_2)_m-N-(amino\ acid)_n-L^1-S-rPE \\ R^1 \\ O$$

$$M = C - X^2 - N$$

AΒ GnRH conjugates I [rPE = reduced Pseudomonas exotoxin linked to L1 via the thiol S; X1 = Leu, Nle; Y = Pro, Hyp; Z = Gly-NH2, D-Ala-NH2, NHEt, NHPr, NHNHCONH2; Q = pGlu-His-Trp, Ac-Phe(Cl-4)-Phe(Cl-4)-Trp, 3-indolylpropionyl; p = 1-2; m = 1-4; n = 0-1; B = CH2, O, S, N; R1 = H, C1-6 alkyl, C3-8 cycloalkyl; (amino acid)n = naturally occurring L-amino acid of its D-stereoisomer; L1 = linker M, COCH2, COCH2CH2S; X2 = C1-5 alkylene, C6H4, C5-6 cycloalkylene] are constructed from GnRH or an analog thereof, a reduced Pseudomonas exotoxin, or a variant thereof, and a unique linking group. The conjugates are administered to male and female animals to sterilize said animals or to reduce tumors that require sex steroids for growth. The instant conjugates are therefore useful as sterilizing agents and anticancer agents. Thus, GnRH analog H-pGlu-His-Tyr-Ser-D-Lys(R)-Leu-Arg-Pro-Gly-NH2 (II; R = H) (solid-phase prepn. given) reacted with .beta.-maleimidopropionic acid N-hydroxysuccinimide ester to give adduct II (R = 3-maleimidopropyl). Reduced Pseudomonas exotoxin PE38QQR was then conjugated to adduct II (R =3-maleimidopropyl).

150954-12-4DP, reaction products with reduced Pseudomonas exotoxin RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of GnRH/reduced Pseudomonas exotoxin conjugates as sterilizing

Parkin 09 623533

and anticancer agents)

150954-12-4P IT

> RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of GnRH/reduced Pseudomonas exotoxin conjugates as sterilizing and anticancer agents)

ANSWER 14 OF 21 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1996:541126 HCAPLUS

DOCUMENT NUMBER:

125:276515

TITLE:

Introduction of the Maleimide Function onto

Resin-Bound Peptides: A Simple, High-Yield Process Useful for Discriminating among Several Lysines

Marburg, S.; Neckers, A. C.; Griffin, P. R.

CORPORATE SOURCE:

Department of Medicinal Chemistry, Merck Research

Laboratories, Rahway, NJ, 07065, USA

SOURCE:

AUTHOR(S):

Bioconjugate Chemistry (1996), 7(5), 612-616.

CODEN: BCCHES; ISSN: 1043-1802

PUBLISHER:

American Chemical Society

DOCUMENT TYPE:

Journal

LANGUAGE: English

Incorporation of Lys(Adpoc) [Adpoc = 1-(1'-adamantyl)-1methylethoxycarbonyl] residues in solid phase peptide synthesis allows selective deprotection of this residue on the resin-bound peptide relative to other acid labile groups such as tert-butoxycarbonyl (Boc). Premature resin cleavage is avoided. A maleimide group, a useful thiol-capture reagent, was readily introduced by reacting the liberated amino function with an acylating agent contg. the maleimide functionality. Acidic cleavage from the resin, with an appropriate scavenging system, afforded peptides that are derivatized with a maleimide functionality on a specific lysine. This is advantageous for producing peptide-carrier conjugates of defined specificity, useful as immunogens, by maleimide-thiol coupling. The derivatization and resin removal chemistries appear to proceed in excellent yield with respect to the maleimide group. The structures were confirmed by tandem mass spectrometry.

ΙT 182250-63-1P 182250-64-2P 182250-65-3P

RL: SPN (Synthetic preparation); PREP (Preparation)

(use of adamantyl (methyl) ethoxycarbonyl protective groups in the solid-phase prepn. of maleimide-substituted lysine-contq. peptides)

ANSWER 15 OF 21 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1995:896110 HCAPLUS

DOCUMENT NUMBER:

123:314539

TITLE:

Preparation of cytotoxic receptor ligand conjugates

linked via lysine radicals.

INVENTOR(S):

Lombardo, Victoria K.; Tolman, Richard L.

PATENT ASSIGNEE(S):

Merck and Co., Inc., USA

SOURCE:

Brit. UK Pat. Appl., 46 pp.

CODEN: BAXXDU

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

APPLICATION NO. PATENT NO. KIND DATE

GB ·2282812

US 1993-138516

19941007

GB 1994-20249

PRIORITY APPLN. INFO.: OTHER SOURCE(S):

MARPAT 123:314539

19950419

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-[Lys(X)]4--Cys-?-Ala-Z
CH<sub>2</sub>
                                        Ι
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AΒ Cytotoxic receptor ligand scaffolds (CRLS) (Lys)n(Unh)m(Sol)m(X)nZ (Unh = sterically unhindered groups; Sol = hydrophilic, solubilizing groups; n = 3-10; m = 0-5; X = receptor ligand; <math>Z = cytotoxin), were prepd. Thus, BrCH2CO-(Lys)4-Cys-.beta.-Ala-OH, prepd. by solid phase synthesis on PAM resin, was stirred in aq. NaHCO3 for 48 h to give cyclic product (I; X =H, Z = OH). This was treated with BrCH2CO2H/DCC to give I (X = COCH2Br, Z = OH), which was coupled to D-Cys6-GnRH in phosphate buffer. The product I (X = COCH2-D-Cys6-GnRH, Z = OH) was coupled with BOC-NHCH2CH2NH2 using BOP/hydroxybenzotriazole followed by deprotection with CF3CO2H/anisole in CH2Cl2 to give I (X = COCH2-D-Cys6-GnRH, Z = NHCH2CH2NH2). This was N-bromoacetylated and conjugated to thiolated exotoxin PE-38M to give a title product contaminated with exotoxin PE-38M. The contaminated product showed a -[log(IC50)] = 8.2 in a competitive binding assay with 125I-buserelin in rat pituitary prepns. The products are claimed for use as chem. sterilants in animals.

ΙT 150954-12-4P

> RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of cytotoxic receptor ligand conjugates linked via lysine radicals)

ANSWER 16 OF 21 HCAPLUS COPYRIGHT 2003 ACS

1995:836656 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 123:309577

Improved tumor targeting with recombinant TITLE:

antibody-macrocycle conjugates

AUTHOR(S): Norman, Timothy J.; Parker, David; Royle, Louise;

> Harrison, Alice; Antoniw, Pari; King, David J. Dep. Chemistry, Univ. Durham, Durham, DH1 3LE, UK

CORPORATE SOURCE: SOURCE: Journal of the Chemical Society, Chemical

Communications (1995), (18), 1877-8

CODEN: JCCCAT; ISSN: 0022-4936 Royal Society of Chemistry

PUBLISHER: DOCUMENT TYPE: Journal

LANGUAGE: English

CASREACT 123:309577 OTHER SOURCE(S):

Linkage of a macrocyclic complexing agent to a spaced tri-maleimide allows formation of a recombinant trivalent antibody by reaction with a .DELTA.-Cys Fab fragment of an engineered human antibody. Given the kinetic stability in vivo of the macrocyclic 90Y complex, the enhanced immunoreactivity of the trivalent recombinant antibody, and the fact that these trivalent antibodies clear rapidly from the blood, indicate the utility of these conjugates for tumor therapy.

146733-82-6D, conjugates with yttrium-90 and antibodies ΙT

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

(Biological study); PROC (Process)

(improved tumor targeting with recombinant antibody-macrocycle conjugates)

ANSWER 17 OF 21 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1995:605782 HCAPLUS

DOCUMENT NUMBER: 123:54133

Annular antigen scaffolds comprising thioether TITLE:

linkages

Parkin 09 623533

INVENTOR(S):

Cunningham, Barry; Hannah, John; Tolman, Richard L.

PATENT ASSIGNEE(S):

Merck and Co., Inc., USA

SOURCE:

Brit. UK Pat. Appl., 51 pp.

CODEN: BAXXDU

DOCUMENT TYPE: LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE GB 2282813 A1 19950419 GB 1994-20263 19941007 PRIORITY APPLN. INFO.: US 1993-138514 19931015

OTHER SOURCE(S):

MARPAT 123:54133

Scaffolds of antigens are prepd. by a convergent synthesis and coupling of sol. precursors comprising solubilizing groups. Cyclic peptide epitopes, known to be more effective immunogen than linear antigens because they are constrained to fewer conformations, are incorporated. In addn. to the epitopes, linear T-haptens may be incorporated at either the C- or the N-terminus of the scaffold construct. The scaffolds constitute effective synthetic vaccines. The scaffolds are cyclized via a thioether linkage, the ring of which comprises from 3 to 10 lysine radicals, to which the epitope or antigen is bonded. The epitope or antigen is preferably and HIV gp120 V3 loop peptide (HIV PND), a malarial peptide, a gonadotropin releasing hormone (GnRH) peptide or bacterial capsular polysaccharide. In example, an annular antigen scaffold core was prepd., conjugated with HIV PND and used for detn. of anti-HIV IgG antibody in sera and antibody induction for neutralizing HIV infectivity, or conjugated with GnRH peptides and used as immunogen and tested for its binding specificity to pituitary GnHR receptor.

IT 150954-12-4P

> RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(annular antigen scaffolds comprising thioether linkages)

T.4 ANSWER 18 OF 21 HCAPLUS COPYRIGHT 2003 ACS

1995:240952 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 122:50243

TITLE: Improved tumor targeting with chemically cross-linked

recombinant antibody fragments

AUTHOR(S): King, David J.; Turner, Alison; Farnsworth, Andrew P.

H.; Adair, John R.; Owens, Raymond J.; Pedley, R.

Barbara; Baldock, Darren; Proudfoot, Karen A.; Lawson,

Alastair D. G.; et al.

CORPORATE SOURCE: Celltech Ltd., Slough, Berkshire, SL1 4EN, UK

SOURCE: Cancer Research (1994), 54(23), 6176-85

CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal LANGUAGE: English

The construction and use of recombinant chimeric and later fully humanized (CDR-grafted) antibodies to tumor-assocd. antigens has reduced the immune response generated to these antibodies in clin. studies. However, their long circulating half-life is a disadvantage for tumor imaging and therapy. Fragments such as F(ab')2, Fab', Fv and single chain Fv (scFv) offer faster blood clearance but also lower overall tumor doses. We have examd. the tumor targeting of several novel fragments produced by chem. crosslinking of Fab' or scFv to dimeric and trimeric species. To facilitate crosslinking of Fab' fragments, a chimeric B72.3 Fab' fragment has been expressed with a hinge sequence contq. a single cysteine residue. B72.3 scFv was also produced with a similar hinge region peptide attached to the COOH terminus to allow crosslinking. These fragments, Fab'.DELTA.Cys and scFv'.DELTA.Cys were cross-linked with linkers contg.

Parkin 09_623533

two or three maleimide groups to produce dimeric and trimeric mols. with increased avidity for antigen. Cross-linkers were also designed to contain a 12-N-4 macrocycle capable of stable radiolabeling with 90Y. This allowed the prodn. of site-specifically-labeled, fully immunoreactive proteins. Biodistribution studies in the nude mouse LS174T xenograft model with scFv, di-scFv, and tri-scFv demonstrated that these fragments clear extremely rapidly from the circulation and give rise to only low levels of activity accumulated at the tumor. Di-Fab (DFM) and tri-Fab (TFM) however, accumulated relatively high levels of activity at the tumor with high tumor:blood ratios generated, demonstrating improved targeting compared to IgG. CB72.3 90Y-labeled tri-Fab was found not to accumulate in the kidney or the bone, resulting in an attractive antibody fragment for tumor therapy.

IT 146733-82-6P 146754-65-6P 146754-67-8P 160176-67-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) \cdot

(tumor targeting for radioimmunotherapy with chem. cross-linked recombinant antibody fragments)

L4 ANSWER 19 OF 21 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1994:23543 HCAPLUS

DOCUMENT NUMBER: 120:23543

TITLE: Chimeric toxins binding to the GnRH receptor

INVENTOR(S): Lombardo, Victoria K.; Tolman, Richard L.; Marburg,

Stephen

PATENT ASSIGNEE(S): Merck and Co., Inc., USA, USA

SOURCE: PCT Int. Appl., 54 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

	PATENT NO.			KIND DATE				APPLICATION NO.						DATE				
	WO 9315751				A1 19930819				WO 1993-US1263					19930212				
		W:								HU,	JP,	KR,	LK,	MG,	MN,	MW,	NO,	NZ,
		RW:						UA, ES.		GB.	GR.	TE.	TT.	T.U.	MC,	NT	PT.	SE.
		-	BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	ML,	MR,	SN,	TD,	ΤG		,	02,
	ΑU	93366	652		A:	1	1993	0903		Α	U 19:	93-30	6652		1993	0212		
	ZA	93009	988	-	A		1993	0920		Z.	A 19	93-98	38		19930	0212		
PRIOR	RITY	APPI	ĹΝ. Ξ	INFO	.:				1	US 1	992-	83603	31	•	1992	0214		
									ì	US 1	993-	9186			19930	0126		
									1	WO 1	993-1	US12	63		19930	0212		

OTHER SOURCE(S): MARPAT 120:23543

Analogs of GnRH are functionalized with unique linking groups so that they may be coupled to a cell-killing mol. The chimeric toxin comprises a GnRH analog, a linking group, and a toxin component. The chimeric toxin is administered to male and female animals where it is transported to organs contg. cells with GnRH receptors such as pituitary glands in order to reduce secretions of sex steroids which results in sterility or in the redn. of tumors that require sex steroids for growth. The compds. are used as sterilizing agents and anticancer agents. The GnRH derivs. modified with the linking groups provide an advantage over prior chimera prepd. by conjugation in that upon amino acid anal. of the conjugate, the modified GnRH deriv. releases an unnatural amino acid which is readily quantified thus reveling the degree of conjugation between the GnRH analog and the toxin. Toxin Pe-38M (Pseudomonas exotoxin A with deletions of residues 1-252 and 365-380, modification at the N-terminus, and 3C-terminal lysines mutated) was recombinantly prepd., thiolated with N-acetylhomocysteine thiolactione, and conjugated with

[N.epsilon.~maleimidopropanoyl)-6-D-Lys]GnRH (prepd. by solid phase peptide synthesis and reaction with .beta.-maleimidopropionic acid N-hydroxysuccinimide ester). During amino acid anal. the linking group breaks down to .beta.-Ala.

IT 150954-12-4P

> RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. and reaction of, with modified exotoxin PE-38M, in prepn. of gonadotropin-releasing hormone analog-toxin conjugate)

ANSWER 20 OF 21 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1993:211310 HCAPLUS

DOCUMENT NUMBER:

118:211310

TITLE:

Tri- and tetra-valent monospecific antigen-binding

proteins

INVENTOR(S):

King, David John; Turner, Alison; Beeley, Nigel Robert

Arnold; Millican, Thomas Andrew

PATENT ASSIGNEE(S):

Celltech Ltd., UK

SOURCE:

PCT Int. Appl., 64 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA'	TENT	NO.		KI	1D	DATE				API	PLIC	CAŤI	ON N	Ο.	DATE	
	9222 9222					1992 1993				WO	199	2-G	B104	 . 7	1992	0611
			•	•		. KR,										
			BE,			DK,							-			SE
AU	9219	716		A1	L	1993	0112			ΑU	199	2-1	9716		1992	0611
EP	5609	47		A1	L	1993	0922			EΡ	199	2-9	1232	9	1992	0611
ĒΡ	5609	47		В1	L	2000	0503									
	R:	GB,	GB,	GB,	GB											
ZA	9204	271	·			1993	1213			ZA	199	2-4	271		1992	0611
JP	0650	2657		T2	2	1994	0324			JΡ	199	2-5	1108	3	1992	0611
JP	3373	849		B2	2	2003	0204									
AT	1924	57		Ε		2000	0515			ΑT	199	2-9	1232	9	1992	0611
ES	2146	212		Т3	3	20000	0801			ES	199	2-9	1232	9	1992	0611
NO	9300	440				1993	0402			NO	199	3-4	40		1993	0209
US	6511	663		В1	_	20030	0128			US	200	0-6	6437	7	20000	
PRIORITY	APP	T.N.	INFO.	:	_			(6	A	1991	
				•									47	A	1992	
															1994	
													15		19950	
СТ								(JO	195	J-4	209	10	DI	1990	7001
GI																

Tri- or tetravalent monospecific antigen-binding proteins comprising 3 or 4 antibody Fab fragments bound covalently to each other by a connecting structure are prepd. A labeling or effector group (e.g. a macrocycle chelating a radioisotope) can be attached and the whole construct can then

```
used in the treatment or diagnosis of, e.g., cancer.
     NHZ(CH2)4CHZNHCOC[(CH2)4NHZ]HNHZ (Z = benzyloxycarbonyl) was dissolved in
     DMSO and N-methylmorpholine was added to the soln. followed by
     succinimidyl maleimido propionate in DMSO. The mixt. was slightly heated
     and the resulting product was worked up and purified to give crosslinking
     agent MalNH(CH2) 4CHZNHCOCH[(CH2) 4NHMal]NHMal (I; Mal = Q; Z = as above).
     Chimeric Fab' fragments of monoclonal antibody B72.3 (specific for tumor-assocd. glycoprotein TAG72), contg. a single hinge thiol group, were
     prepd. and crosslinked the tri-maleimide linker I to make a tri-Fab
     protein. Characterization and biodistribution studies on the tri-Fab
     protein are described. Other tri- and tetra-maleimide linkers were prepd.
     and characterized as well.
     146733-82-6DP, conjugates with Fab fragments of monoclonal
     antibody to tumor-assocd. antigen TAG-72 146754-60-1DP,
     conjugates with Fab fragments of monoclonal antibody to tumor-assocd.
     antigen TAG-72 146754-61-2DP, conjugates with Fab fragments of
     monoclonal antibody to tumor-assocd. antigen TAG-72
     RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
         (prepn. and characterization of)
     146754-65-6P 146754-67-8P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
         (prepn. and reaction of, in maleimide crosslinker synthesis)
     146754-61-2P
     RL: PREP (Preparation)
        (prepn. of, as tetravalent maleimide crosslinker for prepn. of
        tetravalent antibody Fab)
     146733-82-6P 146754-60-1P
     RL: PREP (Preparation)
        (prepn. of, as trivalent maleimide crosslinker for prepn. of trivalent
        antibody Fab)
     ANSWER 21 OF 21 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER:
                          1991:82539 HCAPLUS
DOCUMENT NUMBER:
                          114:82539
                          Use of carboxypeptidase Y for the introduction of
TITLE:
                          probes into proteins via their carboxy terminus
AUTHOR(S):
                          Wilchek, Meir; Schwarz, Alexander; Wandrey, Christian;
                          Bayer, Edward A.
CORPORATE SOURCE:
                          Dep. Biophys., Weizmann Inst. Sci., Rehovot, 76100,
                          Israel
SOURCE:
                          Pept.: Chem., Struct. Biol., Proc. Am. Pept. Symp.,
                          11th (1990), Meeting Date 1989, 1038-40. Editor(s):
                          Rivier, Jean E.; Marshall, Garland R. ESCOM Sci.
                          Pub.: Leiden, Neth.
                          CODEN: 56XTA7
DOCUMENT TYPE:
                          Conference
LANGUAGE:
                          English
     A symposium on the derivatization of protein at their C terminus by
     biocytin amide or N.epsilon.-maleimidopropionyl-L-lysine amide in the
     presence of carboxypeptidase Y.
     132034-12-9
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (derivatization by, of proteins at C-terminus in presence of
        carboxypeptidase Y)
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FILE 'CAOLD' ENTERED AT 15:26:15 ON 20 MAY 2003
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Page 18

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FILE COVERS 1907-1966 FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

=> => s 13 L5 0 L3

=> fil reg FILE 'REGISTRY' ENTERED AT 15:26:28 ON 20 MAY 2003 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2003 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 19 MAY 2003 HIGHEST RN 518003-32-2 DICTIONARY FILE UPDATES: 19 MAY 2003 HIGHEST RN 518003-32-2

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details: http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> => => d sqide 13 1-54

L3 ANSWER 1 OF 54 REGISTRY COPYRIGHT 2003 ACS

RN 475558-10-2 REGISTRY

CN L-Lysinamide, N-[1-oxo-4-(triethylammonio)butyl]glycylglycylglycyl-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 4

NTE modified (modifications unspecified)

SEQ 1 GGGK

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C29 H49 N8 O8

CI COM

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-B

- 1 REFERENCES IN FILE CA (1957 TO DATE)
- 1 REFERENCES IN FILE CAPLUS (1957 TO DATE)
- L3 ANSWER 2 OF 54 REGISTRY COPYRIGHT 2003 ACS
- RN 475558-09-9 REGISTRY
- CN L-Lysinamide, N-[1-oxo-4-(triethylammonio)butyl]glycylgly
- FS PROTEIN SEQUENCE; STEREOSEARCH
- SQL 5

NTE modified (modifications unspecified)

SEQ 1 GGGGK

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C33 H55 N10 O10

CI COM

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.

Parkin 09 623533

PAGE 1-B

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L3 ANSWER 3 OF 54 REGISTRY COPYRIGHT 2003 ACS

RN 446037-14-5 REGISTRY

CN L-Lysinamide, L-histidyl-D-alanyl-L-.alpha.-aspartylglycyl-L-isoleucyl-L-phenylalanyl-L-seryl-L-lysyl-L-alanyl-L-tyrosyl-L-arginyl-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-L-lysyl-L-leucyl-L-leucyl-L-leucyl-L-arginyl-L-asparaginyl-L-glutaminyl-L-leucyl-L-seryl-L-alanyl-L-arginyl-L-asparaginyl-L-tyrosyl-L-leucyl-L-histidyl-L-seryl-L-leucyl-L-methionyl-L-alanyl- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 29

NTE modified (modifications unspecified)

- 2-2-	location			description	
		_	D		

SEQ 1 HADGIFSKAY RKLLGQLSAR NYLHSLMAK

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C155 H244 N46 O41 S

SR CF

LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

PAGE 1-B

PAGE 1-C

PAGE 1-D

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

- 1 REFERENCES IN FILE CA (1957 TO DATE)
- 1 REFERENCES IN FILE CAPLUS (1957 TO DATE)
- L3 ANSWER 4 OF 54 REGISTRY COPYRIGHT 2003 ACS
- RN 446037-12-3 REGISTRY
- CN L-Lysinamide, L-histidyl-D-alanyl-L-.alpha.-aspartylglycyl-L-methionyl-L-phenylalanyl-L-asparaginyl-L-lysyl-L-alanyl-L-tyrosyl-L-arginyl-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-L-lysyl-L-alanyl-L-leucylglycyl-L-glutaminyl-L-leucyl-L-seryl-L-alanyl-L-arginyl-L-lysyl-L-tyrosyl-L-leucyl-L-histidyl-L-seryl-L-leucyl-L-methionyl-L-alanyl- (9CI) (CA INDEX NAME)
- FS PROTEIN SEQUENCE; STEREOSEARCH
- SQL 29

NTE modified (modifications unspecified)

type	location	 	description
stereo	Ala-2	 D ·	·

SEQ 1 HADGMFNKAY RKALGQLSAR KYLHSLMAK

RELATED SEQUENCES AVAILABLE WITH SEQLINK
MF C154 H243 N47 O40 S2

SR CA

LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

PAGE 1-C

PAGE 1-D

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)

1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

ANSWER 5 OF 54 REGISTRY COPYRIGHT 2003 ACS 329716-74-7 REGISTRY L3

RN

CN L-Lysinamide, N-acetyl-L-tyrosylglycylglycyl-L-phenylalanyl-L-leucyl-Larginyl-L-arginyl-L-isoleucyl-L-arginyl-L-prolyl-L-lysyl-L-leucyl-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 8: PN: WO0117568 SEQID: 16 claimed sequence

FS PROTEIN SEQUENCE; STEREOSEARCH

SOL 13

NTE modified (modifications unspecified)

PATENT ANNOTATIONS (PNTE):

Sequence | Patent Source Reference ======+============ Not Given | WO2001017568 1.claimed |SEQID 16

SEQ 1 YGGFLRRIRP KLK

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C84 H134 N26 O18

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

PAGE 1-C

- 1 REFERENCES IN FILE CA (1957 TO DATE)
- 1 REFERENCES IN FILE CAPLUS (1957 TO DATE)
- L3 ANSWER 6 OF 54 REGISTRY COPYRIGHT 2003 ACS
- RN 329716-72-5 REGISTRY
- CN L-Lysinamide, N-[5-[(3aS, 4S, 6aR)-hexahydro-2-oxo-1H-thieno[3, 4-d]imidazol-

Parkin 09 623533

4-yl]-1-oxopentyl]-L-tyrosylglycyl-L-arginyl-L-lysyl-L-lysyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-L-arginyl-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 6: PN: WOO117568 SEQID: 14 claimed sequence

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 12

NTE modified (modifications unspecified)

PATENT ANNOTATIONS (PNTE):

SEQ 1 YGRKKRRQRR RK

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C87 H150 N38 O19 S

SR CA

LC STN Files: C

CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-B

PAGE 1-C

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

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L3 ANSWER 7 OF 54 REGISTRY COPYRIGHT 2003 ACS RN 307315-16-8 REGISTRY
```

CN L-Cysteine, L-seryl-L-alanyl-L-asparaginyl-L-seryl-L-asparaginyl-L-prolyl-L-alanyl-L-methionyl-L-alanyl-L-prolyl-L-arginyl-L-.alpha.-glutamyl-L-arginyl-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-L-lysyl-L-alanylglycyl-L-cysteinyl-L-lysyl-L-asparaginyl-L-phenylalanyl-L-phenylalanyl-L-tryptophyl-L-lysyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-, cyclic (17.fwdarw.28)-disulfide (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 28

NTE modified (modifications unspecified)

```
týpe ----- location ----- description
bridge Cys-17 - Cys-28 disulfide bridge
```

SEQ 1 SANSNPAMAP RERKAGCKNF FWKTFTSC

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C144 H212 N42 O42 S3

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L3 ANSWER 8 OF 54 REGISTRY COPYRIGHT 2003 ACS

RN 307315-11-3 REGISTRY

CN L-Valine, L-cysteinyl-L-asparaginyl-L-leucyl-L-lysyl-L-alpha.-glutamyl-L-alpha.-aspartylglycyl-L-isoleucyl-L-seryl-L-alanyl-L-alanyl-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-L-lysyl-L-alpha.-aspartyl-(9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 14

NTE modified (modifications unspecified)

SEQ 1 CNLKEDGISA AKDV MF C67 H108 N18 O26 S

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

PAGE 2-A

- 1 REFERENCES IN FILE CA (1957 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1957 TO DATE)
- L3 ANSWER 9 OF 54 REGISTRY COPYRIGHT 2003 ACS

RN 307315-10-2 REGISTRY

CN L-Lysine, N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-L-lysyl-L-cysteinyl-L-asparaginyl-L-leucyl-L-lysyl-L-alpha.-glutamyl-L-alpha.-aspartylglycyl-L-isoleucyl-L-seryl-L-alanyl-L-alanyl-L-lysyl-L-alpha.-aspartyl-L-valyl- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 16

NTE modified (modifications unspecified)

SEQ 1 KCNLKEDGIS AAKDVK

MF C79 H132 N22 O28 S

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-A

$$HO_2C$$
 S (CH_2) 4 NH_2
 HO_2C S NH S $Pr-i$
 HO_2C NH NH_2
 HO_2C NH NH_2
 HO_2C NH NH_2
 HO_2C NH NH_2 NH

PAGE 2-A

PAGE 2-B

- 1 REFERENCES IN FILE CA (1957 TO DATE)
- 1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L3 ANSWER 10 OF 54 REGISTRY COPYRIGHT 2003 ACS

RN 307315-09-9 REGISTRY

CN L-Argininamide, L-histidyl-L-alanyl-L-.alpha.-glutamylglycyl-L-threonyl-L-phenylalanyl-L-threonyl-L-seryl-L-.alpha.-aspartyl-L-valyl-L-seryl-L-seryl-L-tyrosyl-L-leucyl-L-.alpha.-glutamylglycyl-L-glutaminyl-L-alanyl-L-alanyl-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-L-lysyl-L-.alpha.-glutamyl-L-phenylalanyl-L-isoleucyl-L-alanyl-L-tryptophyl-L-leucyl-L-valyl-L-lysylglycyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 39: PN: WO0069911 PAGE: 73 claimed protein

FS PROTEIN SEQUENCE; STEREOSEARCH.

SQL 30

NTE modified (modifications unspecified)

PATENT ANNOTATIONS (PNTE):

SEQ 1 HAEGTFTSDV SSYLEGQAAK EFIAWLVKGR

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C156 H231 N41 O48

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.

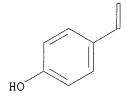
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 H_3
 H_4
 H_4
 H_5
 H_5
 H_6
 H_6
 H_6
 H_7
 H_8
 H_8

PAGE 1-C

PAGE 1-D

PAGE 1-E

PAGE 2-C



2 REFERENCES IN FILE CA (1957 TO DATE)
2 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L3 ANSWER 11 OF 54 REGISTRY COPYRIGHT 2003 ACS

RN 307314-80-3 REGISTRY

CN L-Leucinamide, N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-L-lysyl-L-tyrosylglycylglycyl-L-phenylalanyl-L-leucyl-L-arginyl-L-arginyl-L-isoleucyl-L-arginyl-L-prolyl-L-lysyl- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 13

NTE modified (modifications unspecified)

SEQ 1 KYGGFLRRIR PKL

MF C82 H132 N26 O17

SR CA

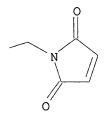
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-B

HO
$$H$$
 S H S H S H S H S H H H

PAGE 1-C



1 REFERENCES IN FILE CARLUS (1957 TO DATE)

1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L3 ANSWER 12 OF 54 REGISTRY COPYRIGHT 2003 ACS

RN 307314-79-0 REGISTRY

CN L-Leucine, N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-L-lysyl-L-tyrosyl-L-prolyl-L-seryl-L-lysyl-L-prolyl-L-alpha.-aspartyl-L-asparaginyl-L-prolylglycyl-L-alpha.-glutamyl-L-alpha.-aspartyl-L-alanyl-L-prolyl-L-alanyl-L-alpha.-glutamyl-L-alpha.-aspartyl-L-methionyl-L-alanyl-L-arginyl-L-tyrosyl-L-tyrosyl-L-seryl-L-alanyl- (9CI) (CA INDEX

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 25

NTE modified (modifications unspecified)

SEQ 1 KYPSKPDNPG EDAPAEDMAR YYSAL

MF C129 H186 N32 O45 S

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

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PAGE 1-D

$$\begin{array}{c|c} H & S & O \\ \hline N & N \\ O & S & (CH_2) 4 & N \\ \hline O & O & O \\ \hline \end{array}$$

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L3 ANSWER 13 OF 54 REGISTRY COPYRIGHT 2003 ACS

RN 307314-78-9 REGISTRY

CN L-Leucine, N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-L-lysyl-L-tyrosyl-L-prolyl-L-seryl-L-lysyl-L-prolyl-L-glutaminyl-L-asparaginyl-L-prolylglycyl-L-alpha.-glutamyl-L-alpha.-aspartyl-L-alanyl-L-prolyl-L-alanyl-L-alpha.-glutamyl-L-alpha.-aspartyl-L-methionyl-L-alanyl-L-arginyl-L-tyrosyl-L-seryl-L-alanyl- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 25

NTE modified (modifications unspecified)

SEQ 1 KYPSKPENPG EDAPAEDMAR YYSAL

MF C130 H188 N32 O45 S

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

PAGE 1-A

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PAGE 1-D

- 1 REFERENCES IN FILE CA (1957 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

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ANSWER 14 OF 54 REGISTRY COPYRIGHT 2003 ACS 307314-73-4 REGISTRY L3

RN

L-Lysinamide, 1-acetyl-L-prolyl-L-arginyl-L-lysyl-L-leucyl-L-tyrosyl-L-CN .alpha.-aspartyl-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-, bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

PROTEIN SEQUENCE; STEREOSEARCH FS

SQL

NTE modified (modifications unspecified)

SEQ 1 PRKLYDK

RELATED SEQUENCES AVAILABLE WITH SEQLINK

C51 H78 N14 O14 . 2 C2 H F3 O2

SR

LC STN Files: CA, CAPLUS, TOXCENTER

CM

CRN 307314-72-3

C51 H78 N14 O14 CMF

Absolute stereochemistry.

PAGE 1-B

$$-NH_2$$
 $(CH_2)_4$
 N
 N
 N
 N

CM 2

76-05-1 CRN

CMF C2 H F3 O2

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L3 ANSWER 15 OF 54 REGISTRY COPYRIGHT 2003 ACS

RN 307314-72-3 REGISTRY

CN L-Lysinamide, 1-acetyl-L-prolyl-L-arginyl-L-lysyl-L-leucyl-L-tyrosyl-L-.alpha.-aspartyl-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-(9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 7

NTE modified (modifications unspecified)

SEQ 1 PRKLYDK

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C51 H78 N14 O14

CI COM

SR CA

PAGE 1-B

$$-NH_2$$
 $(CH_2)_4$
 N
 N
 N
 N

L3 ANSWER 16 OF 54 REGISTRY COPYRIGHT 2003 ACS

RN 307314-71-2 REGISTRY

CN L-Lysinamide, N2-acetyl-L-arginyl-L-lysyl-L-leucyl-L-tyrosyl-L-.alpha.aspartyl-L-tyrosyl-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1oxopropyl]-, bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 7

NTE modified (modifications unspecified)

SEQ 1 RKLYDYK

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C55 H80 N14 O15 . 2 C2 H F3 O2

SR · CA

LC STN Files: CA, CAPLUS, TOXCENTER

CM 1

CRN 307314-70-1 CMF C55 H80 N14 O15

$$H_{2}N$$
 $H_{2}N$
 H

CM 2

CRN 76-05-1 CMF C2 H F3 O2

F-C-CO₂H

- 1 REFERENCES IN FILE CA (1957 TO DATE)
- 1 REFERENCES IN FILE CAPLUS (1957 TO DATE)
- L3 ANSWER 17 OF 54 REGISTRY COPYRIGHT 2003 ACS
- RN 307314-70-1 REGISTRY
- CN L-Lysinamide, N2-acetyl-L-arginyl-L-lysyl-L-leucyl-L-tyrosyl-L-.alpha.-aspartyl-L-tyrosyl-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-

oxopropyl] - (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 7

NTE modified (modifications unspecified)

SEQ 1 RKLYDYK

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C55 H80 N14 O15

CI COM

SR CA

Absolute stereochemistry.

PAGE 1-A

$$H_{2N}$$
 H_{2N}
 H

- L3 ANSWER 18 OF 54 REGISTRY COPYRIGHT 2003 ACS
- RN 307314-69-8 REGISTRY
- CN L-Lysinamide, N2-acetyl-L-arginyl-L-asparaginyl-L-prolyl-L-alpha.-aspartylglycyl-L-alpha.-aspartyl-L-valylglycylglycyl-L-prolyl-L-tryptophyl-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)
- FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 12

NTE modified (modifications unspecified)

SEQ

1 RNPDGDVGGP WK

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C65 H92 N20 O21 . C2 H F3 O2

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

CM 1

CRN 307314-68-7

CMF C65 H92 N20 O21

Absolute stereochemistry.

PAGE 1-A

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PAGE 2-A

CM 2

CRN 76-05-1 CMF C2 H F3 O2

F-C-CO₂H

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L3 ANSWER 19 OF 54 REGISTRY COPYRIGHT 2003 ACS

RN 307314-68-7 REGISTRY

CN L-Lysinamide, N2-acetyl-L-arginyl-L-asparaginyl-L-prolyl-L-.alpha.-aspartylglycyl-L-.alpha.-aspartyl-L-valylglycylglycyl-L-prolyl-L-tryptophyl-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-(9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 12

NTE modified (modifications unspecified)

SEQ 1 RNPDGDVGGP WK

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C65 H92 N20 O21

CI COM

SR CA

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

PAGE 2-A

(CH₂) 3

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RN 307314-67-6 REGISTRY

CN L-Lysinamide, N2-acetyl-L-arginyl-L-asparaginyl-L-prolyl-L-.alpha.aspartylglycyl-L-.alpha.-aspartyl-L-valylglycylglycyl-L-prolyl-Ltryptophyl-L-alanyl-L-tyrosyl-L-threonyl-L-asparaginyl-L-prolylL-arginyl-L-lysyl-L-leucyl-L-tyrosyl-L-.alpha.-aspartyl-L-tyrosyl-N6-[3(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-,
tris(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 24

NTE modified (modifications unspecified)

SEQ 1 RNPDGDVGGP WAYTTNPRKL YDYK

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C134 H191 N37 O41 . 3 C2 H F3 O2

SR CF

LC STN Files: CA, CAPLUS, TOXCENTER

CM 1

CRN 307314-66-5 CMF C134 H191 N37 O41

Absolute stereochemistry.

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PAGE 2-B

CM 2

CRN 76-05-1 CMF C2 H F3 O2

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L3 ANSWER 21 OF 54 REGISTRY COPYRIGHT 2003 ACS

RN 307314-66-5 REGISTRY

CN L-Lysinamide, N2-acetyl-L-arginyl-L-asparaginyl-L-prolyl-L-alpha.aspartylglycyl-L-alpha.-aspartyl-L-valylglycylglycyl-L-prolyl-Ltryptophyl-L-alanyl-L-tyrosyl-L-threonyl-L-threonyl-L-asparaginyl-L-prolylL-arginyl-L-lysyl-L-leucyl-L-tyrosyl-L-alpha.-aspartyl-L-tyrosyl-N6-[3(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]- (9CI) (CA INDEX
NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 24

NTE modified (modifications unspecified)

SEQ. 1 RNPDGDVGGP WAYTTNPRKL YDYK

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C134 H191 N37 O41

CI COM

SR CA

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PAGE 2-B

L3 ANSWER 22 OF 54 REGISTRY COPYRIGHT 2003 ACS

RN 307314-65-4 REGISTRY

CN L-Lysinamide, N-acetyl-L-tyrosyl-L-threonyl-L-threonyl-L-asparaginyl-L-prolyl-L-arginyl-L-lysyl-L-leucyl-L-tyrosyl-L-alpha.-aspartyl-L-tyrosyl-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-, bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 12

NTE modified (modifications unspecified)

SEQ 1 YTTNPRKLYD YK

RELATED SEQUENCES AVAILABLE WITH SEQLINK
MF C81 H116 N20 O24 . 2 C2 H F3 O2

SR

LC STN Files: CA, CAPLUS, TOXCENTER

CM

307314-64-3 CRN

CMF C81 H116 N20 O24

Absolute stereochemistry.

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PAGE 1-B

PAGE 1-C

CM 2

CRN 76-05-1 CMF C2 H F3 O2

- 1 REFERENCES IN FILE CA (1957 TO DATE)
- 1 REFERENCES IN FILE CAPLUS (1957 TO DATE)
- L3 ANSWER 23 OF 54 REGISTRY COPYRIGHT 2003 ACS

RN 307314-64-3 REGISTRY

CN L-Lysinamide, N-acetyl-L-tyrosyl-L-threonyl-L-threonyl-L-asparaginyl-L-prolyl-L-arginyl-L-leucyl-L-tyrosyl-L-alpha.-aspartyl-L-tyrosyl-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 12

NTE modified (modifications unspecified)

SEQ 1 YTTNPRKLYD YK

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C81 H116 N20 O24

CI COM

SR CA

PAGE 1-B

PAGE 1-C

L3 ANSWER 24 OF 54 REGISTRY COPYRIGHT 2003 ACS

RN 307314-63-2 REGISTRY

CN L-Lysinamide, 1-acetyl-L-prolyl-L-arginyl-L-lysyl-L-leucyl-L-tyrosyl-L-.alpha.-aspartyl-L-tyrosyl-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-

Parkin 09 623533

oxopropyl]-, bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME) PROTEIN SEQUENCE; STEREOSEARCH

FS

SQL 8

NTE modified (modifications unspecified)

SEQ 1 PRKLYDYK

RELATED SEQUENCES AVAILABLE WITH SEQLINK

C60 H87 N15 O16 . 2 C2 H F3 O2

SR

LCSTN Files: CA, CAPLUS, TOXCENTER

> CM 1

CRN 307314-62-1 CMF C60 H87 N15 O16

Absolute stereochemistry.

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PAGE 1-B

CM2

CRN 76-05-1 C2 H F3 O2 CMF

1 REFERENCES IN FILE CA (1957 TO DATE)

1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L3. ANSWER 25 OF 54 REGISTRY COPYRIGHT 2003 ACS

RN 307314-62-1 REGISTRY

CN L-Lysinamide, 1-acetyl-L-prolyl-L-arginyl-L-lysyl-L-leucyl-L-tyrosyl-L-.alpha.-aspartyl-L-tyrosyl-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 4: PN: WOO117568 SEQID: 12 claimed protein

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 8

NTE modified (modifications unspecified)

PATENT ANNOTATIONS (PNTE):

SEQ 1 PRKLYDYK

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C60 H87 N15 O16

CI COM

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

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1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

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ANSWER 26 OF 54 REGISTRY COPYRIGHT 2003 ACS
L3
RN
     307314-61-0 REGISTRY
CN
     L-Lysinamide, L-histidyl-L-seryl-L-.alpha.-aspartylglycyl-L-threonyl-L-
     phenylalanyl-L-threonyl-L-seryl-L-.alpha.-glutamyl-L-leucyl-L-seryl-L-
     arginyl-L-leucyl-L-arginyl-L-.alpha.-glutamylglycyl-L-alanyl-L-arginyl-L-
     leucyl-L-.alpha.-glutamyl-L-arginyl-L-leucyl-L-leucyl-L-glutaminylglycyl-L-
     leucyl-L-valyl-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-
           (CA INDEX NAME)
     (9CI)
FS
     PROTEIN SEQUENCE; STEREOSEARCH .
SOL
NTE
    modified (modifications unspecified)
         1 HSDGTFTSEL SRLREGARLE RLLQGLVK
SEO
MF
     C143 H236 N46 O45
SR
     CA
LC
     STN Files:
                 CA, CAPLUS, TOXCENTER
               1 REFERENCES IN FILE CA (1957 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1957 TO DATE)
     ANSWER 27 OF 54 REGISTRY COPYRIGHT 2003 ACS
L3
RN
     307314-59-6 REGISTRY
CN
     L-Lysinamide, L-tyrosyl-L-prolyl-L-seryl-L-lysyl-L-prolyl-L-.alpha.-
     aspartyl-L-asparaginyl-L-prolylglycyl-L-.alpha.-glutamyl-L-.alpha.-
     aspartyl-L-alanyl-L-prolyl-L-alanyl-L-.alpha.-glutamyl-L-.alpha.-aspartyl-
     L-methionyl-L-alanyl-L-arginyl-L-tyrosyl-L-tyrosyl-L-seryl-L-alanyl-L-
     leucyl-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-(9CI)
     (CA INDEX NAME)
FS
     PROTEIN SEQUENCE; STEREOSEARCH
```

Absolute stereochemistry.

STN Files:

C129 H187 N33 O44 S

modified (modifications unspecified)

1 YPSKPDNPGE DAPAEDMARY YSALK

CA, CAPLUS, TOXCENTER

SQL

NTE

SEQ

MF

SR LC

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1 REFERENCES IN FILE CA (1957 TO DATE)

1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L3 ANSWER 28 OF 54 REGISTRY COPYRIGHT 2003 ACS

RN 303013-27-6 REGISTRY

CN L-Lysinamide, N2-acetyl-L-asparaginyl-L-leucyl-L-alpha.-glutamyl-L-alpha.-glutamyl-L-leucyl-L-leucyl-L-lysyl-L-leucyl-L-glutaminyl-L-alpha.-glutamyl-L-alanyl-L-leucyl-L-alpha.-glutamyl-L-lysyl-L-alanyl-L-glutaminyl-L-lysyl-L-leucyl-L-leucyl-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 21

NTE · modified (modifications unspecified)

SEQ 1 NLEELLKKLQ EALEKAQKLL K

MF C121 H207 N31 O36

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.

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R7 R6 HN S Bu-i

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L3 ANSWER 29 OF 54 REGISTRY COPYRIGHT 2003 ACS

RN 287726-97-0 REGISTRY

CN L-Lysinamide, L-tyrosylglycylglycyl-L-phenylalanyl-L-leucyl-L-arginyl-L-arginyl-L-prolyl-L-lysyl-L-leucyl-N6-[3-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)-1-oxopropyl]- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 13

NTE modified (modifications unspecified)

SEQ 1 YGGFLRRIRP KLK

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C86 H134 N26 O17

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

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PAGE 1-C

1 REFERENCES IN FILE CA (1957 TO DATE)

1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

ANSWER 30 OF 54 REGISTRY COPYRIGHT 2003 ACS 274259-01-7 REGISTRY L3

RN

CN L-Lysinamide, N-[1-oxo-4-(triethylammonio)butyl]glycylglycylglycylglycylgl ycyl-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-, bromide (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL

NTE modified (modifications unspecified)

SEQ 1 GGGGGK

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C33 H55 N10 O10 . Br

SR CA

LCSTN Files: CA, CAPLUS

(475558 - 09 - 9)CRN

● Br-

PAGE 1-B

1 REFERENCES IN FILE CA (1957 TO DATE)

1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L3 ANSWER 31 OF 54 REGISTRY COPYRIGHT 2003 ACS

RN 274259-00-6 REGISTRY

CN L-Lysinamide, N-[1-oxo-4-(triethylammonio)butyl]glycylgly

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 5

NTE modified (modifications unspecified)

SEQ 1 GGGGK

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF . C31 H52 N9 O9 . Br

SR CA

LC STN Files: CA, CAPLUS

₽ Br⁻

PAGE 1-B

1 REFERENCES IN FILE CA (1957 TO DATE)

1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

ANSWER 32 OF 54 REGISTRY COPYRIGHT 2003 ACS 274258-99-0 REGISTRY L3

RN

CN L-Lysinamide, N-[1-oxo-4-(triethylammonio)butyl]glycylglycylglycyl-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-, bromide (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SOL

NTE modified (modifications unspecified)

1 GGGK SEQ

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C29 H49 N8 O8 . Br

·SR

LC STN Files: CA, CAPLUS

CRN (475558-10-2)

Br-

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— (CH₂)₃ N+Et3

> 1 REFERENCES IN FILE CA (1957 TO DATE) 1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

ANSWER 33 OF 54 REGISTRY COPYRIGHT 2003 ACS 274258-97-8 REGISTRY L3

RN

CN L-Lysinamide, N-[1-oxo-4-(triethylammonio)butyl]glycylglycyl-N6-[3-(2,5dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-, bromide (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C27 H46 N7 O7 . Br

SR CA

-: -

LC STN Files: CA, CAPLUS

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● Br

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L3 ANSWER 34 OF 54 REGISTRY COPYRIGHT 2003 ACS

RN 274258-95-6 REGISTRY

CN L-Lysinamide, N-[1-oxo-4-(triethylammonio)butyl]glycyl-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-, bromide (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C25 H43 N6 O6 . Br

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.

• Br-

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

- L3 ANSWER 35 OF 54 REGISTRY COPYRIGHT 2003 ACS
- RN 274258-94-5 REGISTRY
- CN 1-Butanaminium, 4-[[1-(aminocarbonyl)-5-[[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]amino]pentyl]amino]-N,N,N-triethyl-4-oxo-, bromide (9CI) (CA INDEX NAME)
- MF C23 H40 N5 O5 . Br
- SR CA

LC STN Files: CA, CAPLUS

• Br

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L3 ANSWER 36 OF 54 REGISTRY COPYRIGHT 2003 ACS

RN 252335-97-0 REGISTRY

CN lH-Pyrrole-1-propanamide, N,N'-[(1S)-1-[[(6-aminohexyl)amino]carbonyl]-1,5-pentanediyl]bis[2,5-dihydro-2,5-dioxo-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C26 H38 N6 O7 . C2 H F3 O2

SR CA

LC STN Files: CA, CAPLUS

CM 1

CRN 252335-96-9 CMF C26 H38 N6 O7

Absolute stereochemistry.

$$\begin{array}{c|c}
O & O & H & NH2 \\
O & O & O & H & NH2 \\
N & S & (CH2) 4 & N & N
\end{array}$$

CM 2

CRN 76-05-1 CMF C2 H F3 O2

- 1 REFERENCES IN FILE CA (1957 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1957 TO DATE)
- L3 ANSWER 37 OF 54 REGISTRY COPYRIGHT 2003 ACS

RN 252335-96-9 REGISTRY

CN 1H-Pyrrole-1-propanamide, N,N'-[(1S)-1-[[(6-aminohexyl)amino]carbonyl]-1,5-pentanediyl]bis[2,5-dihydro-2,5-dioxo-(9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C26 H38 N6 O7

CI . COM

SR CA

Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 ANSWER 38 OF 54 REGISTRY COPYRIGHT 2003 ACS

RN 252335-95-8 REGISTRY

CN Carbamic acid, [6-[[(2S)-2,6-bis[[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]amino]-1-oxohexyl]amino]hexyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C31 H46 N6 O9

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L3 ANSWER 39 OF 54 REGISTRY COPYRIGHT 2003 ACS

224785-62-0 REGISTRY RN

2-12-Dynorphin A (swine), 9a-endo-L-arginine-12-[N6-[3-(2,5-dihydro-2,5-dihyd CN dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-L-lysinamide]- (9CI) (CA INDEX NAME)
PROTEIN SEQUENCE; STEREOSEARCH

FS

SQL

NTE modified (modifications unspecified)

SEQ 1 GGFLRRIRRP KL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

C73 H123 N25 O15 MF

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-A

PAGE 2-A

- 2 REFERENCES IN FILE CA (1957 TO DATE)
- 2 REFERENCES IN FILE CAPLUS (1957 TO DATE)
- L3 ANSWER 40 OF 54 REGISTRY COPYRIGHT 2003 ACS
- RN 224785-55-1 REGISTRY
- CN 1-12-Dynorphin A (swine), 9a-endo-L-arginine-12-[N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-L-lysinamide]-,

pentakis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

- FS PROTEIN SEQUENCE; STEREOSEARCH
- SQL 13

NTE modified (modifications unspecified)

SEQ 1 YGGFLRRIRR PKL

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C82 H132 N26 O17 . 5 C2 H F3 O2

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

CM 1

CRN 224785-54-0

CMF C82 H132 N26 O17

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

PAGE 1-C

CM 2

CRN 76-05-1 CMF C2 H F3 O2

- 2 REFERENCES IN FILE CA (1957 TO DATE) 2 REFERENCES IN FILE CAPLUS (1957 TO DATE)
- ANSWER 41 OF 54 REGISTRY COPYRIGHT 2003 ACS 224785-54-0 REGISTRY L3

RN

CN1-12-Dynorphin A (swine), 9a-endo-L-arginine-12-[N6-[3-(2,5-dihydro-2,5dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-L-lysinamide]- (9CI) (CA INDEX NAME)

PROTEIN SEQUENCE; STEREOSEARCH FS

SQL

NTE modified (modifications unspecified)

SEQ 1 YGGFLRRIRR PKL

RELATED SEQUENCES AVAILABLE WITH SEQLINK.

C82 H132 N26 O17 MF

CI COM

SR CA

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

PAGE 1-C

L3 ANSWER 42 OF 54 REGISTRY COPYRIGHT 2003 ACS

RN 216884-15-0 REGISTRY

CN L-Lysinamide, N2-acetyl-L-asparaginyl-L-leucyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-glutamyl-L-leucyl-L-lysyl-L-lysyl-L-phenylalanyl-L-glutaminyl-L-alpha.-glutamyl-L-alanyl-L-leucyl-L-.alpha.-glutamyl-L-lysyl-L-alanyl-L-leucyl-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 22,21,1 NTE multichain

modified (modifications unspecified)

type ----- location ----- description

bridge Lys-21 - Bal-1' amide bridge uncommon Bal-1' - -

SEQ 1 NLEEFLKKFQ EALEKAQKLL K

SEQ 1 X

MF C127 H203 N31 O36

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A

PAGE 3-A

PAGE 4-A

PAGE 5-A

PAGE 6-A

- 2 REFERENCES IN FILE CA (1957 TO DATE)
- 2 REFERENCES IN FILE CAPLUS (1957 TO DATE)
- . L3 ANSWER 43 OF 54 REGISTRY COPYRIGHT 2003 ACS
 - RN
 - 182250-65-3 REGISTRY L-Threonine, N-[N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-CN alanyl]-L-lysyl]-L-isoleucyl]-L-.alpha.-aspartyl]-L-valyl]-L-lysyl]- (9CI) (CA INDEX NAME)
 - FS PROTEIN SEQUENCE; STEREOSEARCH
 - SQL
 - NTE modified (modifications unspecified)
 - SEQ 1 FEMAKIDVKT
- **RELATED SEQUENCES AVAILABLE WITH SEQLINK** ΜF C60 H93 N13 O19 S

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

- 1 REFERENCES IN FILE CA (1957 TO DATE)
- 1 REFERENCES IN FILE CAPLUS (1957 TO DATE)
- L3. ANSWER 44 OF 54 REGISTRY COPYRIGHT 2003 ACS
- RN 182250-64-2 REGISTRY
- CN L-Threonine, N-[N2-[N-[N-[N-[N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-N2-[N-[N-(N-L-phenylalanyl-L-alpha.-glutamyl)-L-methionyl]-L-alanyl]-L-lysyl]-L-isoleucyl]-L-alpha.-aspartyl]-L-valyl]-L-lysyl]- (9CI) (CA INDEX NAME)
- FS PROTEIN SEQUENCE; STEREOSEARCH
- SQL 10
- NTE modified (modifications unspecified)

SEQ 1 FEMAKIDVKT

- **RELATED SEQUENCES AVAILABLE WITH SEQLINK**
- MF C60 H93 N13 O19 S
- SR CA
- LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A

PAGE 2-A

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- 1 REFERENCES IN FILE CA (1957 TO DATE)
- 1 REFERENCES IN FILE CAPLUS (1957 TO DATE)
- L3 ANSWER 45 OF 54 REGISTRY COPYRIGHT 2003 ACS
- RN 182250-63-1 REGISTRY
- CN Luteinizing hormone-releasing factor (swine), 6-[N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-L-lysine]- (9CI) (CA INDEX NAME) OTHER CA INDEX NAMES:
- CN Luteinizing hormone-releasing factor (pig), 6-[N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-L-lysine]-
- FS PROTEIN SEQUENCE; STEREOSEARCH
- SQL 10

NTE modified (modifications unspecified)

type	location		description
uncommon	Glp-1	-	-

SEQ 1 XHWSYKLRPG

RELATED SEQUENCES AVAILABLE WITH SEQLINK

MF C66 H89 N19 O16

SR CA

LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

- 1 REFERENCES IN FILE CA (1957 TO DATE)
- 1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

```
L3 ANSWER 46 OF 54 REGISTRY COPYRIGHT 2003 ACS
RN 160176-67-0 REGISTRY
CN 1,4,7,10-Tetraazacyclododecane-1,4,7,10-tetraacetic acid,
2-[4-[[2,6-bis[[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-
oxopropyl]amino]-1-oxohexyl]amino]butyl]- (9CI) (CA INDEX NAME)
MF C40 H59 N9 O15
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
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PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L3 ANSWER 47 OF 54 REGISTRY COPYRIGHT 2003 ACS

RN 150954-12-4 REGISTRY

CN Luteinizing hormone-releasing factor (swine), 6-[N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-D-lysine]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:

CN Luteinizing hormone-releasing factor (pig), 6-[N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-D-lysine]-

FS PROTEIN SEQUENCE; STEREOSEARCH

SQL 11,10,1

NTE multichain

modified (modifications unspecified)

type	location		description	
bridge uncommon	Lys-6 Glp-1	- Bal-1'	amide bridge	•
uncommon	Bal-1'	-	-	
stereo	Lys-6	-	D 	

SEQ 1 XHWSYKLRPG

SEQ 1 X

DR 163725-26-6

MF C66 H89 N19 O16

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

- 4 REFERENCES IN FILE CA (1957 TO DATE)
- 1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

4 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L3 ANSWER 48 OF 54 REGISTRY COPYRIGHT 2003 ACS

RN 146754-67-8 REGISTRY

CN L-Lysinamide, N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-L-lysyl-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-L-lysyl-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C39 H54 N10 O12 . C2 H F3 O2

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

CM 1

CRN 146754-66-7 CMF C39 H54 N10 O12

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

CM 2

CRN 76-05-1 CMF C2 H F3 O2

2 REFERENCES IN FILE CA (1957 TO DATE) 2 REFERENCES IN FILE CAPLUS (1957 TO DATE)

ANSWER 49 OF 54 REGISTRY COPYRIGHT 2003 ACS 146754-66-7 REGISTRY L3

RN

L-Lysinamide, N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-L-CN lysyl-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-L-lysyl-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]- (9CI) (CA INDEX

FS STEREOSEARCH

MF C39 H54 N10 O12

CI COM

SR CA

Absolute stereochemistry.

PAGE 1-A

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 ANSWER 50 OF 54 REGISTRY COPYRIGHT 2003 ACS

RN 146754-65-6 REGISTRY

CN L-Lysinamide, N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-N2[(1,1-dimethylethoxy)carbonyl]-L-lysyl-N6-[3-(2,5-dihydro-2,5-dioxo-1Hpyrrol-1-yl)-1-oxopropyl]-L-lysyl-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1yl)-1-oxopropyl]- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C44 H62 N10 O14

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

- 2 REFERENCES IN FILE CA (1957 TO DATE)
 2 REFERENCES IN FILE CAPLUS (1957 TO DATE)
- L3 ANSWER 51 OF 54 REGISTRY COPYRIGHT 2003 ACS
- RN 146754-61-2 REGISTRY
- CN L-Lysine, N2, N6-bis[N2, N6-bis[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-L-lysyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)
- FS STEREOSEARCH
- MF C53 H64 N10 O16
- SR CA
- LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L3 ANSWER 52 OF 54 REGISTRY COPYRIGHT 2003 ACS

RN 146754-60-1 REGISTRY

CN L-Lysine, N2-[N2,N6-bis[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-L-lysyl]-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C40 H47 N7 O12

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

- 1 REFERENCES IN FILE CA (1957 TO DATE)
- 1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
- 1 REFERENCES IN FILE CAPLUS (1957 TO DATE)
- L3 ANSWER 53 OF 54 REGISTRY COPYRIGHT 2003 ACS

RN 146733-82-6 REGISTRY

CN L-Lysinamide, N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-N2[1,4-dioxo-4-[[4-[1,4,7,10-tetrakis(carboxymethyl)-1,4,7,10tetraazacyclododec-2-yl]butyl]amino]butyl]-L-lysyl-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]-L-lysyl-N6-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-1-oxopropyl]- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1,4,7,10-Tetraazacyclododecane, L-lysinamide deriv.

FS STEREOSEARCH

MF C63 H93 N15 O22

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.

PAGE 1-A

PAGE 2-B

но2С

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

- 3 REFERENCES IN FILE CA (1957 TO DATE)
- 2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
- 3 REFERENCES IN FILE CAPLUS (1957 TO DATE)
- L3 ANSWER 54 OF 54 REGISTRY COPYRIGHT 2003 ACS
- RN 132034-12-9 REGISTRY
- CN 1H-Pyrrole-1-propanamide, N-(5,6-diamino-6-oxohexyl)-2,5-dihydro-2,5-dioxo-, (S)- (9CI) (CA INDEX NAME)
- FS STEREOSEARCH
- MF C13 H20 N4 O4
- SR CA
- LC STN Files: CA, CAPLUS

Absolute stereochemistry.

$$\begin{array}{c|c}
 & \text{NH} \\
 & \text{NH} \\
 & \text{O}
\end{array}$$

$$\begin{array}{c|c}
 & \text{NH} \\
 & \text{O}
\end{array}$$

$$\begin{array}{c|c}
 & \text{NH} \\
 & \text{O}
\end{array}$$

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

- 1 REFERENCES IN FILE CA (1957 TO DATE)
 1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

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FILE COVERS 1907 - 20 May 2003 VOL 138 ISS 21 FILE LAST UPDATED: 19 May 2003 (20030519/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> => => d stat que 111 nos 203 SEA FILE=REGISTRY ABB=ON PLU=ON YTSLIHSLIEESQNQQEKNEQELLELDKW L6 ASLWNWF/SQSP 146 SEA FILE=HCAPLUS ABB=ON PLU=ON L6 T.7 113 SEA FILE=HCAPLUS ABB=ON PLU=ON L7(L)(?VIRAL? OR ?VIRU? OR 1.8 HIV?) 57 SEA FILE=HCAPLUS ABB=ON PLU=ON L7 NOT (2003 OR 2002 OR L102001)/PY 39 SEA FILE=HCAPLUS ABB=ON PLU=ON L10 AND L8 L11=> =>

=> s 111 not 14 L12 39 L11 NOT L4

=> d ibib abs hitrn 112 1-39

L12 ANSWER 1 OF 39 HCAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 2001:652880 HCAPLUS

DOCUMENT NUMBER: 135:191275

TITLE: HIV1 gp160 production with recombinant bacteria

INVENTOR(S): Ferreira, Paulo Cesar Peregrino; Kroon, Erna Geessien;

Campos, Marco Antonio da Silva

PATENT ASSIGNEE(S): Universidade Federal de Minas Gerais, Brazil

SOURCE: Braz. Pedido PI, 14 pp.

CODEN: BPXXDX

DOCUMENT TYPE: Patent

LANGUAGE: Portuguese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

Parkin 09_623533 BR 1997-10824 BR 9710824 20000523 19971216 19971216 PRIORITY APPLN. INFO.: BR 1997-10824 Disclosed are HIV1 glycoprotein gp160 and a method for making gp160 by AΒ expressing the gp160 gene in bacteria and recovering the gp160 from the culture. The gp160 may be used in various immunol. methods, such as ELISA, Western blot, etc., for diagnosis. The glycoprotein may also find use as a vaccine to prevent HIV1 infection. Gp160 prodn. with recombinant Escherichia coli is described. IT 239445-66-0P RL: BPN (Biosynthetic preparation); PRP (Properties); BIOL (Biological study); PREP (Preparation) (amino acid sequence; HIV1 gp160 prodn. with recombinant bacteria) L12 ANSWER 2 OF 39 HCAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 2001:24010 HCAPLUS DOCUMENT NUMBER: 134:290001 The possible involvement of CXCR4 in the inhibition of TITLE: HIV-1 infection mediated by DP178/gp41 AUTHOR(S): Xu, Y.; Zhang, X.; Matsuoka, M.; Hattori, T. CORPORATE SOURCE: Laboratory of Virus Immunology, Institute for Virus Research, Kyoto University, Kyoto, 606-8507, Japan SOURCE: FEBS Letters (2000), 487(2), 185-188 CODEN: FEBLAL; ISSN: 0014-5793 Elsevier Science B.V. PUBLISHER: Journal DOCUMENT TYPE: LANGUAGE: English The N- (N36/DP107) and C-terminal peptides (C34/DP178) from two .alpha.-helical domains of human immunodeficiency virus type 1 (HIV-1) gp41 inhibited HIV infection. A single-round infection using pseudotyped virus clarified that a greater amt. of gp41-derived peptides was necessary for the inhibition of R5 virus (ADA) infection than for that of X4 virus (LAI) infection. Furthermore, R5X4 virus (89.6) infection via CCR5 needs more peptides for inhibition than its infection via CXCR4 does. A high sensitivity of X4 virus was partially ascribed to the inhibition of the 12G5 binding to CXCR4 by DP178LAI. ΙT **159519-65-0**, DP178 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (possible involvement of CXCR4 in inhibition of HIV-1 infection mediated by DP178/gp41) REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT L12 ANSWER 3 OF 39 HCAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 2000:847765 HCAPLUS DOCUMENT NUMBER: 134:4044 Varicella-zoster virus carrying HIV env gene for use TITLE: as live vaccines and in chickenpox and AIDS diagnosis Shiraki, Kimiyasu; Takahashi, Masaki INVENTOR(S): Zaidan Hojin Osaka Biseibutsubyo Kenkyu Kai, Japan PATENT ASSIGNEE(S):

SOURCE: Jpn. Kokai Tokkyo Koho, 25 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

JP 2000333678 A2 20001205 JP 1999-104337 19990307
PRIORITY APPLN. INFO.: JP 1999-104337 19990307

AB Recombinant varicella-zoster virus (VZV) expressing HIV gene under the regulation of thymidine kinase (TK) gene promoter is disclosed. Oka varicella vaccine expressing HIV env gene, antigens from it, genomic DNA, live vaccine, and diagnostic reagent, are claimed. Recombinant varicella-zoster virus (VZV) expressing hepatitis B virus (HBV) PreS1, PreS2, and surface antigen (HBs) was constructed and examd. for its immunogenicity in guinea-pigs. Similarly, recombinant VZV expressing HIV env gene was constructed. Antigens from the recombinant VZV were used as diagnostic reagents for chickenpox and hepatitis B. Avirulent vaccines induced cellular immunity in chickenpox and AIDS.

IT 308310-41-0

RL: PRP (Properties)

(unclaimed sequence; varicella-zoster virus carrying HIV env gene for use as live vaccines and in chickenpox and AIDS diagnosis)

L12 ANSWER 4 OF 39 HCAPLUS COPYRIGHT 2003 ACS 2000:755939 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER:

134:275224

TITLE:

New mechanism of action of anti-HIV drugs: T20 or

DP178

AUTHOR(S):

Hattori, Toshio

CORPORATE SOURCE:

Graduate School of Medical Science, Tohoku University,

Japan

SOURCE:

Chiryogaku (2000), 34(9), 1016-1018

CODEN: CHRYDT; ISSN: 0386-8109

PUBLISHER:

Raifu Saiensu Shuppan K.K.

DOCUMENT TYPE:

Journal; General Review

LANGUAGE:

Japanese

A review, with 5 refs., discussing the effect of the new anti-HIV1 drug T20 or DP178 on gp41 glycoproteins.

IT. **159519-65-0**, DP178

> RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(new mechanism of action of anti-HIV drugs: T20 or DP178).

L12 ANSWER 5 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

2000:642426 HCAPLUS

DOCUMENT NUMBER:

133:305320

TITLE:

Sensitivity of human immunodeficiency virus type 1 to the fusion inhibitor T-20 is modulated by coreceptor

specificity defined by the V3 loop of gp120

AUTHOR(S):

SOURCE:

Derdeyn, Cynthia A.; Decker, Julie M.; Sfakianos, Jeffrey N.; Wu, Xiaoyun; O'Brien, William A.; Ratner, Lee; Kappes, John C.; Shaw, George M.; Hunter, Eric Department of Microbiology, University of Alabama at

CORPORATE SOURCE:

· Birmingham, Birmingham, AL, 35294, USA

Journal of Virology (2000), 74(18), 8358-8367

CODEN: JOVIAM; ISSN: 0022-538X American Society for Microbiology

PUBLISHER: DOCUMENT TYPE:

Journal LANGUAGE: English

T-20 is a synthetic peptide that potently inhibits replication of human immunodeficiency virus type 1 by interfering with the transition of the transmembrane protein, gp41, to a fusion active state following interactions of the surface glycoprotein, gp120, with CD4 and coreceptor mols. displayed on the target cell surface. Although T-20 is postulated to interact with an N-terminal heptad repeat within gp41 in a trans-dominant manner, the authors show here that sensitivity to T-20 is strongly influenced by coreceptor specificity. When 14 T-20-naive primary isolates were analyzed for sensitivity to T-20, the mean 50% inhibitory concn. (IC50) for isolates that utilize CCR5 for entry (R5 viruses) was

0.8 log10 higher than the mean IC50 for CXCR4 (X4) isolates. Using NL4.3-based envelope chimeras that contain combinations of envelope sequences derived from R5 and X4 viruses, the authors found that determinants of coreceptor specificity contained within the gp120 V3 loop modulate this sensitivity to T-20. The IC50 for all chimeric envelope viruses contg. R5 V3 sequences was 0.6 to 0.8 log10 higher than that for viruses contg. X4 V3 sequences. In addn., the authors confirmed that the N-terminal heptad repeat of gp41 dets. the baseline sensitivity to T-20and that the IC50 for viruses contg. GIV at amino acid residues 36 to 38 was 1.0 log10 lower than the IC50 for viruses contg. a G-to-D substitution. The results of this study show that gp120-coreceptor interactions and the gp41 N-terminal heptad repeat independently contribute to sensitivity to T-20. These results have important implications for the therapeutic uses of T-20 as well as for unraveling the complex mechanisms of virus fusion and entry.

IT **159519-65-0**, T-20

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(sensitivity of human immunodeficiency virus type 1 to the gp41 fusion inhibitor T-20 is modulated by coreceptor specificity defined by V3 loop of gp120)

REFERENCE COUNT:

THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS 60 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

HCAPLUS COPYRIGHT 2003 ACS L12 ANSWER 6 OF 39

ACCESSION NUMBER: DOCUMENT NUMBER:

2000:553429 HCAPLUS 133:147459

TITLE:

HIV drug resistance system

INVENTOR(S):

Kappes, John C.; Wu, Xiaoyun; Shaw, George M.

PATENT ASSIGNEE(S):

UAB Research Foundation, The, USA

SOURCE:

PCT Int. Appl., 22 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

```
APPLICATION NO. DATE
PATENT NO.
               KIND DATE
                                    WO 2000-US2643
WO 2000045833
               A1
                      20000810
   W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
       DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP,
       KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO,
       NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA,
       UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
   RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
       DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
       CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                  US 1999-118283P · P 19990202
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PRIORITY APPLN. INFO.: T-20, a synthetic peptide corresponding to the 2nd heptad repeat (HR2) of HIV-1 gp41, blocks HIV-1 entry at nanogram concns. in vitro. To look for genetic evidence of virus selection and possible resistance development, population sequencing of plasma vRNA (cDNA) was performed at 0, 10, and 14 days of therapy by a method previously described (Nature 373:117, 1995). In 1 of 4 subjects treated with intermediate drug doses (30 mg bid), there was a major shift in the viral quasispecies within HR1 at amino acid position 36 (G to D). Mol. cloning and sequencing of 52 individual vRNA(cDNA) envelope clones from this subject confirmed this change in 50% of clones; in addn., other amino acid substitutions were identified at positions 36 (G to S), 32 (Q to R/H), 38 (V to A), and 39 (Q to R) as well as double mutations at 32, 36, and/or 39.

ΙT 159519-65-0

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(HIV drug resistance system)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 7 OF 39 HCAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 2000:406756 HCAPLUS

DOCUMENT NUMBER: 133:144541

TITLE: The HIV-1 Cell Entry Inhibitor T-20 Potently

Chemoattracts Neutrophils by Specifically Activating

the N-Formylpeptide Receptor

AUTHOR(S): Hartt, Jennifer K.; Liang, Thomas; Sahagun-Ruiz,

Alfredo; Wang, Ji-Ming; Gao, Ji-Liang; Murphy, Philip

Μ.

CORPORATE SOURCE: Laboratory of Host Defenses, National Institute of

Allergy and Infectious Diseases, National Institutes

of Health, Bethesda, MD, 20892, USA

SOURCE: Biochemical and Biophysical Research Communications

(2000), 272(3), 699-704

CODEN: BBRCA9; ISSN: 0006-291X

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal LANGUAGE: English

T-20, a synthetic peptide corresponding to the heptad repeat sequence of HIV-1 gp41, blocks HIV-1 entry by targeting gp41, and is currently in clin. trials as an anti-retroviral agent. The authors recently reported that in vitro T-20 also functions as a phagocyte chemoattractant and a chemotactic agonist at the phagocyte N-formylpeptide receptor (FPR). the authors show that T-20 is also a potent chemotactic agonist in vitro at a related human phagocyte receptor FPRL1R. To test the relative importance of FPR and FPRL1R in primary cells, the authors identified the corresponding mouse T-20 receptors, mFPR and FPR2, which are both expressed in neutrophils, and compared T-20 action on neutrophils from wild type and mFPR knockout mice. Surprisingly, although T-20 activates mFPR and FPR2 in transfected cells with equal potency and efficacy in both calcium flux and chemotaxis assays, neutrophils from mFPR knockout mice did not respond to T-20. These results provide genetic evidence that FPR is the major phagocyte T-20 receptor in vivo and point to the potential feasibility of studying T-20 effects on immunity in a mouse model. This may help define the cause of local inflammation after T-20 injection that has recently been reported in Phase I clin. trials. (c) 2000 Academic

IT **159519-65-0**, T-20

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(HIV-1 cell entry inhibitor T-20 potently chemoattracts

neutrophils by specifically activating N-formylpeptide receptor in

relation to inflammation)

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 8 OF 39 HCAPLUS COPYRIGHT 2003 ACS ACCESSION NUMBER: 2000:119743 HCAPLUS

DOCUMENT NUMBER: 132:288345

TITLE: Sensitivity to a nonpeptidic compound (RPR103611)

blocking human immunodeficiency virus type 1 Env-mediated fusion depends on sequence and

accessibility of the gp41 loop region

AUTHOR(S): Labrosse, Beatrice; Treboute, Carole; Alizon, Marc

CORPORATE SOURCE: INSERM U.332, Institut Cochin de Genetique

Moleculaire, Paris, 75014, Fr.

SOURCE: Journal of Virology (2000), 74(5), 2142-2150

CODEN: JOVIAM; ISSN: 0022-538X American Society for Microbiology

DOCUMENT TYPE: Journal LANGUAGE: English

PUBLISHER:

The triterpene RPR103611 is an efficient inhibitor of membrane fusion mediated by the envelope proteins (Env, gp120-gp41) of CXCR4-dependent (X4) human immunodeficiency virus type 1 (HIV-1) strains, such as HIV-1LAI (LAI). Other X4 strains, such as HIV-1NDK (NDK), and CCR5-dependent (R5) HIV-1 strains, such as HIV-1ADA (ADA), were totally resistant to RPR103611. Anal. of chimeric LAI-NDK Env proteins identified a fragment of the NDK gp41 ectodomain detg. drug resistance. A single difference at position 91, leucine in LAI and histidine in NDK, apparently accounted for their sensitivity or resistance to RPR103611. The authors had previously identified a mutation of isoleucine 84 to serine in a drug escape LAI variant. Both I84 and L91 are located in the "loop region" of gp41 sepg. the proximal and distal helix domains. Nonpolar residues in this region therefore appear to be important for the antiviral activity of RPR103611 and are possibly part of its target. However, another mechanism had to be envisaged to explain the drug resistance of ADA, since its gp41 loop region was almost identical to that of LAI. Fusion mediated by chimeric Env consisting of LAI gp120 and ADA gp41, or the reciprocal construct, was fully blocked by RPR103611. The gp120-gp41 complex of R5 strains is stable, relative to that of X4 strains, and this stability could play a role in their drug resistance. Indeed, when the postbinding steps of ADA infection were performed under mildly acidic conditions (pH 6.5 or 6.0), a treatment expected to favor dissocn. of gp120, the authors achieved almost complete neutralization by RPR103611. The drug resistance of NDK was partially overcome by preincubating virus with sol. CD4, a gp120 ligand inducing conformational changes in the Env complex. The antiviral efficacy of RPR103611 therefore depends on the sequence of the gp41 loop and the stability of the gp120-gp41 complex, which could limit the accessibility of this target.

IT 264584-24-9

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(amino acid sequence; sensitivity to a nonpeptidic compd. (RPR103611)

blocking human immunodeficiency virus type 1 Env-mediated

fusion depends on sequence and accessibility of gp41 loop region in

relation to stability of gp120-gp41 complex)

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 9 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:46951 HCAPLUS

DOCUMENT NUMBER:

132:118353

TITLE:

Methods for the detection of non-pathogenic HIV-1 strains containing deletions in the nef coding region

and U3 region of the LTR

INVENTOR(S):

Deacon, Nicholas John; McPhee, Dale Alan; Crowe,

Suzanne

PATENT ASSIGNEE(S):

The MacFarlane Burnet Centre for Medical Research

Ltd., Australia

SOURCE:

U.S., 308 pp., Cont.-in-part of U.S. Ser. No.

388,353.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.

KIND DATE

APPLICATION NO. DATE

US 6015661 US 1995-488551 Α 20000118 19950607 US 6010895 US 1995-388353 20000104 Α 19950214 PRIORITY APPLN. INFO.: US 1995-388353 19950214 AU 1995-3021 19950517

AΒ The present invention is directed toward immunol.- and nucleic acid-based methodologies for the detection of non-pathogenic human immunodeficiency virus type 1 (HIV-1) strains in the body fluids of HIV-infected individuals. A blood donor infected with HIV-1 and a cohort of 6 blood or blood product recipients infected from this donor were studied. These patients, who remained free of HIV-1-related disease and displayed stable and normal CD4 lymphocyte counts 10-14 yr after infection, were termed long-term nonprogressors (LTNPs). The mol. characterization of HIV-1 sequences obtained from either virus isolates or patient peripheral blood mononuclear cells (PBMCs) of LTNPs identified similar deletions in the nef gene and in the region of overlap of nef and the U3 region of the long terminal repeat (LTR). These deletions corresponded to amino acids 166-206, or nucleotides 9281 to 9437, of the HIV-1NL43 nef/LTR region. Methods were developed to detect the presence of nonpathogenic HIV-1 strains carrying these deletions in HIV-infected patients.

IT 169874-95-7

RL: ADV (Adverse effect, including toxicity); ANT (Analyte); PRP (Properties); ANST (Analytical study); BIOL (Biological study) (amino acid sequence; methods for the detection of non-pathogenic HIV-1 strains contg. deletions in the nef coding region and U3 region of the LTR)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 10 OF 39 HCAPLUS COPYRIGHT 2003 ACS

2000:39264 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER:

132:317484

TITLE:

SOURCE:

The emerging role of fusion inhibitors in HIV

infection

AUTHOR(S):

De Clercq, Erik

CORPORATE SOURCE:

Rega Institute for Medical Research, Katholieke

Universiteit Leuven, Louvain, Belg. Drugs in R&D (1999), 2(5), 321-331 CODEN: DRDDFD; ISSN: 1174-5886

Adis International Ltd.

PUBLISHER: DOCUMENT TYPE:

Journal; General Review

LANGUAGE: English

A review with 47 refs. Fusion of HIV with its host cell requires the interaction of the viral envelope glycoprotein 120 (gp 120) with the chemokine receptor CXCR4 [T cell-tropic (T-tropic) or X4 HIV strains] or CCR5 [macrophage-tropic (M-tropic) or R5 HIV strains] followed by a "spring-loaded" action of the glycoprotein 41 (gp41) that ensures fusion of the viral and cellular lipid membranes and permits the viral nucleocapsid to enter the cell. The overall fusion process can be blocked by a no. of compds. These include siamycin analogs, SPC 3 (a synthetic peptide derived from the V3 domain of gp120), pentafuside (T 20, DP 178) [a synthetic peptide corresponding to amino acid residues 127 to 162 of gp41], the betulinic acid deriv. RPR 103611, TAK 779 (a low mol. wt. non-peptide CCR5 antagonist) and a no. of compds. (T 22, T 134, ALX40-4C, CGP64222 and AMD 3100) that are targeted at the CXCR4 receptor. In particular, the bicyclam AMD 3100 has proved highly potent and selective as a CXCR4 antagonist that blocks the infectivity of X4 HIV strains in the nanomolar concn. range. The proof-of-concept that fusion inhibitors should be able to suppress viral replication in vivo has been demonstrated with pentafuside. Pentafuside and AMD 3100 have now proceeded to phase II clin. trials.

IT **159519-65-0**, Pentafuside

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(the emerging role of fusion inhibitors in HIV infection)

47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT:

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 11 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

2000:12484 HCAPLUS

DOCUMENT NUMBER:

132:247579

TITLE:

Inhibition of HIV-1 Entry Before gp41 Folds Into its

Fusion-active Conformation Kliger, Yossef; Shai, Yechiel

AUTHOR(S): CORPORATE SOURCE:

Department of Biological Chemistry, The Weizmann

SOURCE:

Institute of Science, 76100, Israel Journal of Molecular Biology (2000), 295(2), 163-168

CODEN: JMOBAK; ISSN: 0022-2836

PUBLISHER:

Academic Press

DOCUMENT TYPE:

Journal LANGUAGE: English

AB HIV-1 entry into its host cell is modulated by its transmembrane envelope glycoprotein (gp41). The core of the activated conformation of gp41 consists of a trimer of heterodimers comprising a leucine/isoleucine zipper sequence (represented here by the synthetic peptide N36 or by the longer N51 peptide) and a C-terminal highly conserved region (represented here by C34). A correlation was found between the action of DP178, which is a potent inhibitor of HIV-1 entry into its host cell, and its ability to interact with the leucine/isoleucine zipper sequence. This correlation was further tested and confirmed by CD spectroscopy. We found that whereas DP178 perturbs the partial .alpha.-helix nature of peptides corresponding to the leucine/isoleucine zipper sequence (N36 or N51), it cannot perturb the trimer of heterodimers conformation, modeled by the complex of N36 or N51 with C34. Therefore, we suggest that the already formed trimer of heterodimers is not the target of inhibition by DP178. Our results are consistent with a model in which DP178 acquires its inhibitory activity by binding to an earlier intermediate of gp41, in which the N and C peptide regions are not yet assocd., thus allowing DP178 to bind to the leucine/isoleucine zipper sequence and consequently to inhibit transition to the fusion-active conformation. (c) 2000 Academic Press.

ΙT 159519-65-0

> RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(inhibition of HIV-1 entry before gp41 folds into its

fusion-active conformation)

REFERENCE COUNT:

THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS 41 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 12 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

2000:10566 HCAPLUS

DOCUMENT NUMBER:

132:74538

TITLE:

Non-pathogenic strains of HIV-1 containing mutations in the nef gene or the U3 region of the long terminal

INVENTOR(S):

repeat Deacon, Nicholas John; Learmont, Jennifer Catherine;

PATENT ASSIGNEE(S):

McPhee, Dale Alan; Crowe, Suzanne; Cooper, David Macfarlane Burnet Centre for Medical Research Limited,

Australia; Australian Red Cross Society

SOURCE:

U.S., 243 pp.

CODEN: USXXAM

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6010895	A	20000104	US 1995-388353	19950214
US 6015661	Α.	20000118	US 1995-488551	19950607
PRIORITY APPLN. INFO.	:		US 1995-388353	19950214
			AU 1995-3021	19950517

This invention is directed toward non-pathogenic human immunodeficiency AΒ virus type 1 (HIV-1) strains contg. deletions in the nef gene and U3 region of the long terminal repeat (LTR). A blood donor infected with HIV-1 and a cohort of 6 blood or blood product recipients infected from this donor were identified. These individuals, who remained free of HIV-1-related disease with stable and normal CD4+ lymphocyte counts 10-14 yr after infection, were termed long-term nonprogressors (LTNPs). The mol. characterization of HIV-1 sequences obtained from either virus isolates or patient peripheral blood mononuclear cells (PBMCs) of LTNPs identified similar deletions in the nef gene and in the region of overlap of nef and the U3 region of the LTR. Full-length sequencing of one isolate genome and amplification of selected HIV-1 genome regions from other cohort members revealed no other abnormalities of obvious functional significance. These deletions corresponded to amino acids 166-206, or nucleotides 9281-9437, of the HIV-1NL43 nef/LTR region. These data illustrate the importance of nef or the U3 region of the LTR in detg. the pathogenicity of HIV-1. These non-pathogenic strains should prove useful, inter alia, in the development of HIV-1-specific diagnostic reagents.

ΙT 169874-95-7

RL: PRP (Properties)

(unclaimed protein sequence; non-pathogenic strains of HIV-1 contg. mutations in the nef gene or the U3 region of the long terminal

REFERENCE COUNT:

THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 13 OF 39 HCAPLUS COPYRIGHT 2003 ACS 1999:674767 HCAPLUS ACCESSION NUMBER:

13

DOCUMENT NUMBER:

TITLE:

Selection of gp41-mediated HIV-1 cell entry inhibitors

from biased combinatorial libraries of non-natural

binding elements

AUTHOR(S):

Ferrer, Marc; Kapoor, Tarun M.; Strassmaier, Tim; Weissenhorn, Winfried; Skehel, John J.; Oprian, Dan; Schreiber, Stuart L.; Wiley, Don C.; Harrison, Stephen

C.

CORPORATE SOURCE:

Department of Molecular and Cellular Biology, Harvard

University, Cambridge, MA, 02138, USA

SOURCE:

Nature Structural Biology (1999), 6(10), 953-960

CODEN: NSBIEW; ISSN: 1072-8368

PUBLISHER:

. Nature America

DOCUMENT TYPE:

Journal LANGUAGE: English

The trimeric, .alpha.-helical coiled-coil core of the HIV-1 gp41 AB ectodomain is thought to be part of a transient, receptor-triggered intermediate in the refolding of the envelope glycoprotein into a fusion-active conformation. In an effort to discover small org. inhibitors that block gp41 activation, we have generated a biased combinatorial chem. library of non-natural binding elements targeted to the gp41 core. From this library of 61,275 potential ligands, we have identified elements that, when covalently attached to a peptide derived from the gp41 outer-layer .alpha.-helix, contribute to the formation of a stable complex with the inner core and to inhibition of gp41-mediated cell fusion.

ΙT **159519-65-0**, DP-178

RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); BIOL (Biological study)

(selection of gp41-mediated HIV-1 cell entry inhibitors from biased combinatorial libraries of non-natural binding elements)

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 14 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:577149 HCAPLUS

DOCUMENT NUMBER: 131:180832

TITLE: Process to produce recombinant protein gp160 of human

immunodeficiency virus

INVENTOR(S): Ferreira, Paulo Cesar Peregrino; Kroon, Erna Geessien;

·Campos, Marco Antonio da Silva

PATENT ASSIGNEE(S): Universidade Federal de Minas Gerais, Brazil

SOURCE: Braz. Pedido PI, 11 pp.

CODEN: BPXXDX

DOCUMENT TYPE: Patent LANGUAGE: Portuguese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

BR 9700856 A 19981215 BR 1997-856 19970102

PRIORITY APPLN. INFO.: BR 1997-856 19970102

AB The present invention describes recombinant gp160 protein derived from the human immunodeficiency virus 1, and the process of prodn. of the recombinant protein using genetic engineering techniques, to be used in immunodiagnosis (such as ELISA) or in vaccines. Thus, DNA sequences encoding the hybrid protein were amplified, fractionated, purified, and cloned on plasmid vectors for expression in appropriate bacteria.

IT 239445-66-0D, gp160 (human immunodeficiency virus-1)
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP
 (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU
 (Occurrence); USES (Uses)

(process for expression and prodn. of recombinant protein gp160 derived from human immunodeficiency viruses (HIV-1))

L12 ANSWER 15 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:458586 HCAPLUS

DOCUMENT NUMBER: 131:294951

TITLE: Pentafuside (Trimeris)

AUTHOR(S): Press, Natasha; Hedberg, Brad; Conway, Brian CORPORATE SOURCE: Departments of Medicine and Pharmacology &

Therapeutics, Viridae Clinical Sciences, University of

British Columbia, Vancouver, BC, V6Z 1Y8, Can.

SOURCE: IDrugs (1999), 2(7), 702-710

CODEN: IDRUFN; ISSN: 1369-7056

PUBLISHER: Current Drugs Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 92 refs. Pentafuside (T-20) is a 36-amino-acid peptide compd. under development by Trimeris for the potential treatment of HIV infection, for which it received US FDA fast track designation in Feb. 1999. It corresponds to amino acids 638-673 of HIV-1(LA1) transmembrane protein gp41. Pentafuside blocks HIV infection, uniquely, by preventing membrane fusion, an essential process in viral replication. In preclin. studies it blocked infection of cells by HIV and prevented the fusion of one HIV-infected cell with another. In Mar. 1998, Trimeris signed a letter of intent with DuPont Merck Pharm Co to conduct trials of Merck's efavirenz in combination with pentafuside. The trial planned to enroll up to 48 HIV-infected individuals at three sites in the US, who have begun to fail their existing triple combination therapy. Prior exposure to

nonnucleoside reverse transcriptase inhibitors and protease inhibitors, other than indinavir, will be among the exclusion criteria for the study. The 1st 10 days of the study is a dose-optimization period that will assess the safety, pharmacokinetics and antiviral activity of multiple ascending doses of pentafuside. After completion of this period, subjects will be eligible to participate in an extension period of at .gtoreq.6 mo, during which pentafuside will be administered in combination with efavirenz and two protease inhibitors. The use of pentafuside and truncated peptides in combination with other antiviral agents is claimed in WO-09640191.

IT **159519-65-0P**, Pentafuside

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(pharmacol. of pentafuside as **antiviral** compd. in human **HIV** infection)

REFERENCE COUNT:

52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 16 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1999:413560 HCAPLUS

DOCUMENT NUMBER:

131:222921

TITLE:

Pentafuside Trimeris

AUTHOR(S):

Press, Natasha; Hedberg, Brad; Conway, Brian

CORPORATE SOURCE: Departments

Departments of Medicine and Pharmacology & Therapeutics Viridae Clinical, University of British

Columbia, Vancouver, BC, V6Z 1Y8, Can.

SOURCE:

Current Opinion in Anti-Infective Investigational

Drugs (1999), 1(2), 171-178 CODEN: COADFY; ISSN: 1464-8458

PUBLISHER:

Current Drugs Ltd.

DOCUMENT TYPE: Journal; General Review

LANGUAGE:

English

Pentafuside (T-20) is a 36 amino acid peptide A review with many refs. under development by Trimeris for the potential treatment of HIV infection, for which it received US FDA fast track designation in Feb. 1999 [313596,182694]. It corresponds to amino acids 638 to 673 of HIV-1(LA1) transmembrane protein, gp41 [238873]. Pentafuside blocks HIV infection, uniquely, by preventing membrane fusion, an essential process in viral replication. In preclin. studies, it blocked infection of cells by HIV and prevented the fusion of one HIV-infected cell with another [171217]. In Mar. 1998, Trimeris signed a letter of intent with DuPont Merck Pharm Co to conduct trials of Merck's efavirenz in combination with pentafuside. The trial planned to enroll .ltoreq.48 HIV-infected individuals at three sites in the US, who have begun to fail their existing triple combination therapy. Prior exposure to non-nucleoside reverse transcriptase inhibitors and protease inhibitors, other than indinavir, will be among the exclusion criteria for the study. The first 10 days of the study are a dose-optimization period that will assess the safety, pharmacokinetics and antiviral activity of multiple ascending doses of pentafuside. After completion of this period, subjects will be eligible to participate in an extension period of at least six months, during which pentafuside will be administered in combination with efavirenz and two protease inhibitors [281696]. The use of pentafuside and truncated peptides in combination with other antiviral agents is claimed in WO-09640191.

IT **159519-65-0**, Pentafuside

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(pentafuside development by Trimeris for HIV infection treatment in humans)

L12 ANSWER 17 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:347451 HCAPLUS

DOCUMENT NUMBER:

131:143434

· TITLE:

T20/DP178, an ectodomain peptide of human

immunodeficiency virus type 1 gp41, is an activator of

human phagocyte N-formyl peptide receptor

AUTHOR(S):

Su, Shao Bo; Gong, Wang-Hua; Gao, Ji-Liang; Shen, Wei-Ping; Grimm, Michael C.; Deng, Xiyun; Murphy, Philip M.; Oppenheim, Joost J.; Wang, Ji Ming

CORPORATE SOURCE:

Laboratory of Molecular Immunoregulation, Division of

Basic Sciences, and Intramural Research Support

Program, SAIC Frederick, National Cancer

Institute-Frederick Cancer Research and Development

Center, Frederick, MD, 21702-1201, USA

SOURCE:

Blood (1999), 93(11), 3885-3892 CODEN: BLOOAW; ISSN: 0006-4971

W. B. Saunders Co. PUBLISHER:

DOCUMENT TYPE:

Journal

LANGUAGE: English .

Human immunodeficiency virus type 1 (HIV-1) envelope protein gp41 mediates viral fusion with human host cells. The peptide segment T20/DP178, located in the C-terminus of the ectodomain of gp41, interacts with the N-terminal leucine zipper-like domain on gp41 to establish the fusogenic conformation of the virus. Synthetic T20/DP178 peptide is highly efficacious in inhibiting HIV-1 infection in vitro by disrupting the transformation of fusogenic status of viral gp41; thus, it has been proposed for clin. trial. The authors report that synthetic T20/DP178 is a chemoattractant and activator of human peripheral blood phagocytes but not of T lymphocytes. The authors further demonstrate that T20/DP178 specifically activates a seven-transmembrane, G-protein-coupled phagocyte receptor for N-formylated chemotactic peptides, formyl peptide receptor (FPR). Moreover, synthetic T20/DP178 analogs lacking N-terminal amino acids acted as FPR antagonists. The results suggest that gp41 peptides regulate phagocyte function via FPR and identify a novel mechanism by which HIV-1 may modulate innate immunity.

IT 235787-61-8

> RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(ectodomain peptide of human immunodeficiency virus type 1

gp41 is activator and chemoattractant for human phagocytes via formyl peptide receptor)

REFERENCE COUNT:

47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 18 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:732698 HCAPLUS

DOCUMENT NUMBER:

TITLE:

Potent suppression of HIV-1 replication in humans by T-20, a peptide inhibitor of gp41-mediated virus entry

AUTHOR(S):

Kilby, J. Michael; Hopkins, Sam; Venetta, Thomas M.; DiMassimo, Betty; Cloud, Gretchen A.; Lee, Jeannette Y.; Alldredge, Leslie; Hunter, Eric; Lambert, Dennis; Bolognesi, Dani; Matthews, Thomas; Johnson, M. Ross; Nowak, Martin A.; Shaw, George M.; Saag, Michael S.

CORPORATE SOURCE:

Dep. Med., Univ. Alabama at Birmingham, Birmingham,

AL, 35294-2050, USA

SOURCE:

Nature Medicine (New York) (1998), 4(11), 1302-1307

CODEN: NAMEFI; ISSN: 1078-8956

PUBLISHER:

Nature America

DOCUMENT TYPE:

Journal

LANGUAGE: English T-20, a synthetic peptide corresponding to a region of the transmembrane subunit of the HIV-1 envelope protein, blocks cell fusion and viral entry at concns. of less than 2 ng/mL in vitro. We administered i.v. T-20 (monotherapy) for 14 days to sixteen HIV-infected adults in four dose groups (3, 10, 30 and 100 mg twice daily). There were significant, dose-related declines in plasma HIV RNA in all subjects who received higher dose levels. All four subjects receiving 100 mg twice daily had a decline in plasma HIV RNA to less than 500 copies/mL, by bDNA assay. A sensitive RT-PCR assay (detection threshold 40 copies/mL) demonstrated that, although undetectable levels were not achieved in the 14-day dosing period, there was a 1.96 log10 median decline in plasma HIV RNA in these subjects. This study provides proof-of-concept that viral entry can be successfully blocked in vivo. Short-term administration of T-20 seems safe and provides potent inhibition of HIV replication comparable to anti-retroviral regimens approved at present. ΙT 159519-65-0, T-20 Peptide RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (potent suppression of HIV-1 replication in humans by T-20, a peptide inhibitor of gp41-mediated virus entry) THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: 49 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT L12 ANSWER 19 OF 39 HCAPLUS COPYRIGHT 2003 ACS 1998:481908 HCAPLUS ACCESSION NUMBER: DOCUMENT NUMBER: 129:235586 TITLE: In vitro study of alginate/chitosan microspheres for controlled release of the anti-HIV drug T20 AUTHOR(S): Yan, C.; Zhang, H.; Lambert, D. M.; Ussery, M. A.; Nielsen, C. J. CORPORATE SOURCE: Enterprise Technology Solutions, LC, Frederick, MD, 21702, USA SOURCE: Proceedings of the International Symposium on Controlled Release of Bioactive Materials (1998), 25th, 510-511 CODEN: PCRMEY; ISSN: 1022-0178 PUBLISHER: Controlled Release Society, Inc. DOCUMENT TYPE: Journal LANGUAGE: English T20 (a peptide) was encapsulated into alginate/chitosan microspheres by an aq. diffusion method providing a significantly slower release rate of the drug than the control. **159519-65-0**, T20 RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (in vitro study of alginate/chitosan microspheres for controlled release of anti-HIV drug T20) REFERENCE COUNT: THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT L12 ANSWER 20 OF 39 HCAPLUS COPYRIGHT 2003 ACS 1998:275963 HCAPLUS ACCESSION NUMBER: DOCUMENT NUMBER: 129:36036 TITLE: Quantitation of a 36-amino-acid peptide inhibitor of HIV-1 membrane fusion in animal and human plasma using high-performance liquid chromatography and

fluorescence detection AUTHOR(S):

Lawless, Mary K.; Hopkins, Sam; Anwer, Mohmed K.

Trimeris, Inc., Durham, NC, 27707, USA CORPORATE SOURCE:

Journal of Chromatography, B: Biomedical Sciences and SOURCE:

Applications (1998), 707(1 + 2), 213-217

CODEN: JCBBEP; ISSN: 0378-4347

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal LANGUAGE: English

Selective extn. of a 36-amino-acid peptide (DP-178, T20, pentafuside) from AB the protein matrixes of animal and human plasma was achieved using acetonitrile contg. 1% trifluoroacetic acid and 1% n-nonyl-.beta.-Dglucopyranoside. The peptide concn. of the ext. was measured using reversed-phase high-performance liq. chromatog. (RP-HPLC) and fluorescence detection. The eluent was excited at 280 nm and the intrinsic fluorescence signal was collected at 350 nm. Recovery of T20 from the plasma matrixes was 75% (mouse), 60% (rat), 50% (cynomolgus monkey), and 55% (human) based on parallel-processed aq. T20 std. solns. The fluorescence peak area vs. concn. of T20 was linear in the range 4-160 ng/mL based on the final solute concn. in the HPLC vial, corresponding to original plasma concns. of 100-4000 ng/mL. Expts. with truncated analogs of T20 demonstrate that this assay offers the advantage of detecting metabolites attributable to bio-transformation degrdn. processes differing by as little as one amino acid from the original peptide.

159519-65-0P, T 20 IT

> RL: ANT (Analyte); PUR (Purification or recovery); ANST (Analytical study); PREP (Preparation)

(detn. of pentafuside, inhibitor of ${\bf HIV}\text{--}1$ membrane fusion, in animal and human plasma using HPLC and fluorescence detection)

THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: 10

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 21 OF 39 HCAPLUS COPYRIGHT 2003 ACS 1998:232468 HCAPLUS

ACCESSION NUMBER:

129:2665 DOCUMENT NUMBER:

TITLE: Capture of an early fusion-active conformation of

HIV-1 gp41

Furuta, Rika A.; Wild, Carl T.; Weng, Yongkai; Weiss, AUTHOR(S):

Carol D.

Center for Biologics Evaluation and Research (CBER), CORPORATE SOURCE:

Food and Drug Administration (FDA), Office of

Vaccines, Bethesda, MD, 20892-4555, USA

Nature Structural Biology (1998), 5(4), 276-279 SOURCE:

CODEN: NSBIEW; ISSN: 1072-8368

PUBLISHER: Nature America

DOCUMENT TYPE: Journal LANGUAGE: English

Using an inhibitory synthetic peptide (DP-178) from HIV-1 gp41, HIV-1 envelope glycoprotein (Env) undergoing conformational changes during virus entry was trapped. Data show that DP-178 binds gp41 and inhibits Env-mediated membrane fusion after gp 120 interacts with cellular receptors, indicating that conformational changes involving the coiled coil domain of gp41 are required for entry. Capture of this fusion-active conformation of Env provides insights into the early events leading to Env-mediated membrane fusion.

159519-65-0, DP-178 ΙT

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

(capture of an early fusion-active conformation of HIV-1

gp41)

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 22 OF 39 HCAPLUS COPYRIGHT 2003 ACS

1998:64927 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 128:203975

Dilation of the human immunodeficiency virus-1 TITLE:

envelope glycoprotein fusion pore revealed by the inhibitory action of a synthetic peptide from gp41 Munoz-Barroso, Isabel; Durell, Stewart; Sakaguchi,

Kazuyasu; Appella, Ettore; Blumenthal, Robert

Laboratory of Experimental and Computational Biology, CORPORATE SOURCE: National Institutes of Health, Frederick, MD, USA

Journal of Cell Biology (1998), 140(2), 315-323

SOURCE:

CODEN: JCLBA3; ISSN: 0021-9525

PUBLISHER: Rockefeller University Press

DOCÚMENT TYPE: Journal LANGUAGE: English

AUTHOR(S):

The authors monitored fusion between cell pairs consisting of a single human immunodeficiency virus-1 (HIV-1) envelope glycoprotein-expressing cell and a CD4+ target cell, which had been labeled with both a fluorescent lipid in the membrane and a fluorescent solute in the cytosol. The authors developed a new 3-color assay to keep track of the cell into which fluorescent lipids and/or solutes are redistributed. Lipid and solute redistribution occur as a result of opening a lipid-permissive fusion pore and a solute-permissive fusion pore (FPs), resp. A synthetic peptide (DP178) corresponding to residues 643-678 of the HIV-1LAI gp120-gp41 sequence (Wild, C.T., et al., 1994) completely inhibited FPs at 50 ng/mL, whereas at that concn. there was 20-30% fusion activity measured by the lipid redistribution. The differences detected in lipid mixing vs. contents mixing are maintained up to 6 h of coculture of gp120-41-expressing cells with target cells, indicating that DP178 can "clamp" the fusion complex in the lipid mixing intermediate for very long time periods. A peptide from the N-terminal of gp41, DP107, inhibited HIV-1LAI gp120-gp41-mediated cell fusion at higher concns., but with no differences between lipid and aq. dye redistribution at the different inhibitor concns. The inhibition of solute redistribution by DP178 was complete when the peptide was added to the fusion reaction mixt. during the first 15 min of coculture. The authors have analyzed the inhibition data in terms of a fusion pore dilation model that incorporates the recently detd. high resoln. structure of the gp41 core.

IT · 159519-65-0

AUTHOR(S):

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study) (HIV-1 envelope glycoprotein fusion pore dilation revealed by inhibitory action of synthetic peptide from gp41)

L12 ANSWER 23 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:52533 HCAPLUS

DOCUMENT NUMBER: 128:203868

TITLE: Determinants of human immunodeficiency virus type 1

> resistance to gp41-derived inhibitory peptides Rimsky, Laurence T.; Shugars, Diane C.; Matthews,

Thomas J.

Department of Surgery, Duke University Medical Center, CORPORATE SOURCE:

Durham, NC, 27710, USA

Journal of Virology (1998), 72(2), 986-993 SOURCE:

CODEN: JOVIAM; ISSN: 0022-538X American Society for Microbiology

PUBLISHER: DOCUMENT TYPE: Journal LANGUAGE: English

A synthetic peptide, DP178, contg. amino acids 127-162 of the human immunodeficiency virus type 1 ($H\bar{I}V-1$) gp41 Env glycoprotein, is a potent inhibitor of virus infection and virus mediated cell-to-cell fusion (C. Wild, et al., 1993). In an effort to understand the mechanism of action of this peptide, the authors derived resistant variants of $\operatorname{HIV-1IIIB}$ and NL4-3 by serial virus passage in the presence of increasing doses of the peptide. Sequence anal. of the resistant isolates suggested that a

contiguous 3-amino-acid sequence within the N-terminal heptad repeat motif of gp41 was assocd. with resistance. Site-directed mutagenesis studies

confirmed this observation and indicated that changes in 2 of these 3 residues were necessary for development of the resistant phenotype. Direct binding of DP178 to recombinant protein and synthetic peptide analogs contg. the wild-type and mutant heptad repeat sequences revealed a strong correlation between DP178 binding and the biol. sensitivity of the corresponding virus isolates to DP178. The results are discussed from the standpoints of the mechanism of action of DP178 and recent crystallog. information for a core structure of the gp41 ectodomain.

IT 159519-65-0

RL: PRP (Properties)

(determinants of human immunodeficiency virus type 1 resistance to gp41-derived inhibitory peptide DP178)

L12 ANSWER 24 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1997:802576 HCAPLUS

DOCUMENT NUMBER:

128:123475

TITLE:

Inhibition of HIV type 1 infectivity by constrained .alpha.-helical peptides: implications for the viral

fusion mechanism

AUTHOR (S):

Judice, J. Kevin; Tom, Jeffrey Y. K.; Huang, Wei;

Wrin, Terri; Vennari, Joann; Petropoulos, Christos J.;

McDowell, Robert S.

CORPORATE SOURCE:

Dep. Bioorga. Chem., Genentech, Inc., South San

Francisco, CA, 94080, USA

SOURCE:

Proceedings of the National Academy of Sciences of the United States of America (1997), 94(25), 13426-13430

CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER:

National Academy of Sciences

DOCUMENT TYPE:

Journal English

LANGUAGE:

Linear peptides derived from the membrane proximal region of the gp41 ectodomain are effective inhibitors of HIV type 1 (HIV-1)-mediated fusion events. These inhibitory peptides lack structure in soln., rendering mechanistic interpretation of their activity difficult. Using structurally constrained analogs of these mols., we demonstrate that the peptides inhibit infectivity by adopting a helical conformation.

Moreover, we show that a specific face of the helix must be exposed to

peptides inhibit infectivity by adopting a helical conformation. Moreover, we show that a specific face of the helix must be exposed to block viral infectivity. Recent crystal structures show that the region of gp41 corresponding to the inhibitory peptides is helical and uses the analogous face to pack against a groove formed by an N-terminal coiled-coil trimer. Our results provide a direct link between the inhibition of HIV-1 infectivity by these peptides and the x-ray structures, and suggest that the conformation of gp41 obsd. by crystallog. represents the fusogenic state. Other agents that block HIV-1 infectivity

by binding to this groove may hold promise for the treatment of AIDS. IT 159519-65-0

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(inhibition of **HIV** type 1 infectivity by constrained .alpha.-helical peptides: implications for the **viral** fusion

mechanism)

L12 ANSWER 25 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1996:593984 HCAPLUS

DOCUMENT NUMBER:

125:270178

TITLE:

HIV-1 membrane fusion mechanism: structural studies of the interactions between biologically-active peptides

from gp41

AUTHOR(S):

Lawless, Mary K.; Barney, Shawn; Guthrie, Kelly I.; Bucy, Teresa B.; Petteway, Stephen R., Jr.; Merutka,

Gene

CORPORATE SOURCE:

Trimeris Inc., Research Triangle Park, NC, 27709, USA

SOURCE:

Biochemistry (1996), 35(42), 13697-13708

CODEN: BICHAW; ISSN: 0006-2960

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal LANGUAGE: English

Two synthetic peptides corresponding to sequences in HIV-1LAI gp41, T21 (aa 558-595) and T20 (aa 643-678), are strong inhibitors of HIV-1 viral fusion, having EC50 values of 1 .mu.g/mL and 1 ng/mL, resp. Previous work suggested that T21 forms a coiled-coil structure in PBS soln., while T20 is primarily nonhelical, and that the inhibitory action of these peptides occurs after the interaction between the viral gp120 protein and the cellular CD4 receptor. The current study uses sedimentation equil. (SE), CD, and viral-fusion assays to quant. investigate peptide structure and peptide-peptide interactions. SE analyses of T21 (1-100 .mu.M) indicate that the peptide self-assocs. via a monomer/dimer/tetramer equil.; in addn., T20 is monomeric in the range of 1-10 .mu.M and exhibits a complicated monomer/tetramer equil. between 20 and 100 .mu.M. Singular value decompn. analyses of the CD spectra of T21 and T20 indicate that the helical content of these peptides in PBS soln. is 90% and 20%, resp. A structural interaction between the 2 peptides is detected by CD at several concn. ratios of T20:T21. These expts. emphasize that T20 interacts specifically with the tetrameric form of T21. Truncated forms of T20 also exhibit structural interactions with T21 at varying concn. ratios. The ability of T20 and the truncated peptides to interact structurally with tetrameric T21 correlates with antiviral activity. Implications of these findings are discussed in terms of proposed mechanisms of membrane fusion inhibition and the structural changes which occur in gp41 during membrane fusion.

IT 159519-65-0

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(HIV-1 membrane fusion mechanism: structural studies of the interactions between biol.-active peptides from gp41)

L12 ANSWER 26 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1996:386031 HCAPLUS

DOCUMENT NUMBER: 125:50774

TITLE: A recombinant protein designated DEV-1, useful in the

detection of HIV virus, DNA sequence encoding the protein, and human blood viral infection diagnosis

using immunoassay

INVENTOR(S): Devash, Yair
PATENT ASSIGNEE(S): Devaron, Inc., USA
SOURCE: PCT Int. Appl., 36 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT	NO.	KI	ND	DATE			A	PPLI	CATI	N NC	٥.	DATE			
WO 9612	023	 A	1	19960	0425		W	0 19	95-U	s133	35	- - 1995	1011		
W:	AL, A	M, AT,	ΑU,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CZ,	DE,	DK,	EE,	ES,
	FI, G	B, GE,	HU,	IS,	JP,	ΚE,	KG,	ΚP,	KR,	ΚZ,	LK,	LR,	LT,	LU,	LV,
•	MD, M	G, MK,	MN,	MW,	MX,	NO,	ΝZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,
	SK, T	J													
RW:	KE, M	W, SD,	SZ,	UG,	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IE,	ΙΤ,
	LU, M	C, NL,	PT,	SE,	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	ML,	MR,	NE,
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AB Purified protein DEV-1, and biol. active analogs, fragments and derivs.

thereof are described, which are useful, inter alia as an antigen for the detection of HIV antibodies in human biol. samples.

ΙT 178038-95-4P

> RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses) (amino acid sequence; recombinant protein designated DEV-1, useful in

detection of HIV virus, DNA sequence encoding protein, and human blood viral infection diagnosis using immunoassay)

L12 ANSWER 27 OF 39 HCAPLUS COPYRIGHT 2003 ACS

1995:896324 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER:

123:310209

TITLE:

INVENTOR(S):

Non-pathogenic strains of HIV-1

Deacon, Nicholas John; Learmont, Jennifer Catherine; McPhee, Dale Alan; Crowe, Suzanne; Cooper, David

Macfarlane Burnet centre for Medical Research,

PATENT ASSIGNEE(S):

Australia; Australian Red Cross Society

SOURCE:

PCT Int. Appl., 302 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION: PATENT NO

	PAT	rent :	NO.		KI	ND	DATE				PPLI				DATE				
	WO	9521	912		 A:	1									1995	0214			
		W:	AM,	ΑT,	AU,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CZ,	DE,	DK,	ΕE,	ES,	FI,	
			GB,	GE,	HU,	JP,	ΚE,	KG,	ΚP,	KR,	ΚZ,	LK,	LR,	LT,	LU,	LV,	MD,	MG,	
			MN,	MW,	MX,	NL,	NO,	ΝZ,	PL,	PT,	RO,	RU,	SD,	SE,	SI,	SK,	ТJ,	TT,	
			UA,	UG															
		RW:	ΚE,	MW,	SD,	SZ,	UG,	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	ΙE,	ΙT,	
			LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	ML,	MR,	NE,	
			SN,	TD,	TG														
	CA	2183	154		A	A	1995	0817		C	A 19	95-2	1831	54	1995	0214		2	
		9517								P	U 19	95-1	7008		1995	0214			
	ΑU	6991	75		B	2	1998	1126											
	ZA	9501	182		Α		1995	1018		Z	A 19	95-1	182		1995	0214			
	ΕP	7542																	
															LU,				SE
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									1	WO 1	995-	AU63		W	1995	0214			

The present invention relates to non-pathogenic strains of HIV-1 and to components, parts, fragments and derivs. thereof and to genetic sequences derived therefrom and their use in the development of diagnostic and therapeutic compns. for the treatment and prophylaxis of AIDS and AIDS-related disorders. The present invention also relates to a method for attenuating pathogenic strains of HIV-1 by mutagenizing particular regions of the HIV-1 genome.

169874-95-7 TΤ

RL: PRP (Properties)

(amino acid sequence; nonpathogenic strains of HIV-1)

L12 ANSWER 28 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1995:882934 HCAPLUS

DOCUMENT NUMBER:

124:46731

TITLE:

Recovery of virtually full-length HIV-1 provirus of diverse subtypes from primary virus cultures using the

polymerase chain reaction

AUTHOR(S): Salminen, Mika O.; Koch, Christine; Sanders-Buell,

Eric; Ehrenberg, Philip K.; Michael, Nelson L.; Carr,

Jean K.; Burke, Donald S.; McCutchan, Francine E. CORPORATE SOURCE: Henry M. Jackson Foundation for Advancement Military

Med., Rockville, MD, 20850, USA Virology (1995), 213(1), 80-6 CODEN: VIRLAX; ISSN: 0042-6822

PUBLISHER: Academic DOCUMENT TYPE: Journal LANGUAGE: English

AB In the course of the global pandemic, the human immunodeficiency virus type-1 (HIV-1) has established .gtoreq.8 distinct genotypes in the main (M), or prevalent, group of isolates, a variety of rare outlier forms, and intergenotypic recombinants of group M viruses. This genotypic diversity has been documented, for the most part, by sequencing of subgenomic segments of the provirus. DNA from virus cultures on peripheral blood mononuclear cells (PBMC) and recent improvements of the PCR technique were used to amplify virtually full-length HIV-1 genomes from genetic subtypes A through G of group M viruses and several of them were molecularly cloned. Resequencing of the complete genome of a prototype strain after long PCR amplification and cloning has established a PCR error rate of The first complete PCR-derived sequence of a U.S. clin. isolate of genotype B expanded only in primary PBMC is also reported; this provirus harbors a uniquely truncated V3 loop.

IT 171886-27-4

SOURCE:

RL: PRP (Properties)

(amino acid sequence; recovery of virtually full-length HIV-1 provirus of diverse subtypes from primary virus cultures using PCR)

L12 ANSWER 29 OF 39 HCAPLUS COPYRIGHT 2003 ACS

1995:698894 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 123:76420

TITLE:

A method of encapsidating poliovirus nucleic acids lacking genes essential for encapsidation and uses of

the encapsidated nucleic acids

INVENTOR(S): Morrow, Casey D.

PATENT ASSIGNEE(S): UAB Research Foundation, USA

SOURCE: Can. Pat. Appl., 62 pp.

CODEN: CPXXEB

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2125344	AA	19950102	CA 1994-2125344	19940607
US 5622705	A	19970422	US 1995-444882	19950519
US 5614413	A	19970325	US 1996-589446	19960122
ORITY APPLAL INFO) . •		US 1993-87009 A	19930701

A method of encapsidating a recombinant poliovirus nucleic acid lacking some of the functions necessary for encapsidation is described. The method involves a host cell line that carries an expression vector that complements the defect in the poliovirus. The poliovirus nucleic acid is introduced into the host cells and and is packaged. A foreign nucleotide sequence is generally substituted for the nucleotide sequence of the poliovirus nucleic acid encoding at least a portion of a protein necessary for encapsidation. The encapsidated virus may be used to synthesize a foreign antigen and so act as the immunogenic component of a vaccine. HeLa or BSC40 cells transformed with a vaccinia virus expression vector carrying the poliovirus P1 precursor gene were transformed with the

transcript of a chimeric poliovirus genome with the VP2 or VP3 regions substituted with the HIV-1 gag or pol genes and the virus recovered from cell lysates. Mice inoculated with these constructs developed an immune response to the HIV-1 antigen.

ΙT 165308-52-1

> RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(amino acid sequence; method of encapsidating poliovirus nucleic acids lacking genes essential for encapsidation and uses of encapsidated nucleic acids)

L12 ANSWER 30 OF 39 HCAPLUS COPYRIGHT 2003 ACS

1995:364733 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER:

122:281521

TITLE:

Interactions of HIV-1 envelope glycoproteins with

derivatized dextrans

AUTHOR(S):

Carre, Vincent; Mbemba, Elisabeth; Letourneur, Didier;

Jozefonvicz, Jacqueline; Gattegno, Liliane

CORPORATE SOURCE:

Laboratoire de Biologie Cellulaire, Faculte de

Medecine, Universite Paris-Nord, 74 Rue Marcel Cachin,

Bobigny, 93012, Fr.

SOURCE:

Biochimica et Biophysica Acta (1995), 1243(2), 175-80

CODEN: BBACAQ; ISSN: 0006-3002

PUBLISHER:

Journal

Elsevier DOCUMENT TYPE: LANGUAGE: English

Derivatized dextrans, such as carboxylmethyl dextran benzylamide and carboxymethyl dextran benzylamide sulfonate, specifically interacted with HIV-1 envelope glycoproteins (rgp160 and rgp41) with significantly higher affinities than those obsd. for dextran sulfate (MW 8 kDa). These results suggest the possible involvement in HIV infectivity of surface membrane mols. which may bind the virus at pre or post-CD4 binding steps. They also suggest the possible use of these compds. in anti-HIV therapy.

IT 162995-83-7 162995-84-8

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(amino acid sequence; interactions of HIV-1 envelope glycoproteins with derivatized dextrans in relation to antiviral activity)

L12 ANSWER 31 OF 39 HCAPLUS COPYRIGHT 2003 ACS 1995:122836 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER:

122:2742

TITLE:

Peptides corresponding to a predictive .alpha.-helical domain of human immunodeficiency virus type 1 gp41 are

potent inhibitors of virus infection

AUTHOR(S):

Wild, Carl T.; Shugars, Diane C.; Greenwell, Teresa

K.; McDanal, Charleen B.; Matthews, Thomas J.

CORPORATE SOURCE:

Dep. Surg., Duke Univ. Med. Cent., Durham, NC, 27710,

USA

SOURCE:

Proceedings of the National Academy of Sciences of the

United States of America (1994), 91(21), 9770-4

CODEN: PNASA6; ISSN: 0027-8424

DOCUMENT TYPE:

Journal English

LANGUAGE:

To define the role of the human immunodeficiency virus type 1 (HIV-1) envelope proteins in virus infection, a series of peptides were synthesized based on various regions of the HIV-1 transmembrane protein gp41. One of these peptides, DP-178, corresponding to a region predictive of .alpha.-helical secondary structure (residues 643-678 of the HIV-1LAI isolate), has been identified as a potent antiviral agent. This peptide consistently blocked 100% of virus-mediated cell-cell fusion at <5 ng/mL (IC90 .apprxeq. 1.5 ng/mL) and gave an .apprxeq. 10 times redn. in

infectious titer of cell-free virus at .apprxeq.80 ng/mL. The inhibitory activity was obsd. at peptide concns. .apprxeq. 104 to 104 times lower than those at which cytotoxicity and cytostasis were detected. Peptide-mediated inhibition is HIV-1 specific in that .apprxeq.102 to 103 times more peptide was required for inhibition of a human immunodeficiency virus type 2 isolate. Further expts. showed that DP-178 exhibited antiviral activity against both prototypic and primary HIV-1 isolates. As shown by PCR anal. of newly synthesized proviral DNA, DP-178 blocks an early step in the virus life cycle prior to reverse transcription. Finally, the authors discuss possible mechanisms by which DP-178 may exert its inhibitory activity.

IT 159519-65-0

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(corresponding to predictive .alpha.-helical domain of human immunodeficiency virus type 1 gp41 are potent inhibitors of virus infection)

L12 ANSWER 32 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1994:595914 HCAPLUS

DOCUMENT NUMBER: 121:195914

TITLE: Deletion mutants of the gp41 glycoprotein of human

immunodeficiency virus 1 and their use in the

treatment of HIV-1 infection

INVENTOR(S): Essex, Myron E.; Yu, Xiaofang; Lee, Tun Hou

PATENT ASSIGNEE(S): Harvard College, USA SOURCE: PCT Int. Appl., 53 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE WO 9412533 A1 19940609 WO 1993-US212 19930112 W: CA, JP RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE 19940609 CA 1993-2150028 19930112 CA 2150028 AA EP 1993-903064 EP 674657 Α1 19951004 R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE US 5736391 19980407 US 1995-467933 19950606 Α PRIORITY APPLN. INFO.: US 1992-979975 19921123 WO 1993-US212 19930112

Deletion mutants of glycoprotein gp41 of HIV-1 are characterized for use in the treatment of HIV-1 infection. Mutants of HIV-1 with deletions in the C-terminal region of gp41 were constructed without interfering with the overlapping rev gene and COS-7 cells were transfected with the DNA to generate the virus. When the viruses were used to infect T-lymphoid cell lines, it was found that replication was dramatically impaired with all but one of the mutants failing to establish productive infection with the infectivity of the most productive strain 2 logs lower than that of the wild type. Immunoblots of viral proteins from virions showed normal levels of gag p24, and p17, pol p66, p51, and p34 but dramatically lower levels of gp120 and gp41.

IT 158130-86-0 158130-87-1 158130-88-2 158130-89-3 158130-90-6 158130-91-7

RL: PRP (Properties)

(amino acid sequence of, for treatment of HIV infection, prepn. of)

IT 158130-85-9D, C-terminal deletion analogs

RL: PROC (Process)

(for treatment of HIV infection, prepn. of)

L12 ANSWER 33 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1993:3468 HCAPLUS

DOCUMENT NUMBER:

118:3468

TITLE:

Molecular characterization of biologically diverse

envelope variants of human immunodeficiency virus type

1 derived from an individual

AUTHOR(S): CORPORATE SOURCE:

Daniels, Rod S.; Smith, Marian H.; Fisher, Amanda G. Virol. Div., Natl. Inst. Med. Res., London, NW7 1AA,

SOURCE:

Journal of Virology (1991), 65(10), 5574-8

CODEN: JOVIAM; ISSN: 0022-538X

DOCUMENT TYPE:

Journal

LANGUAGE:

English

The envelope genes of 6 viruses derived from a single sampling from an individual chronically infected with human immunodeficiency virus type 1 (RJS-4) were analyzed. The nucleotide and predicted amino acid sequences of these variants are given and a correlation between biol. properties and disturbance of the envelope reading frame.

144903-86-6, Glycoprotein (human immunodeficiency provirus ΙT 1 clone pHXB2gpt gene env precursor protein moiety reduced)

RL: PRP (Properties)

(amino acid sequence of)

L12 ANSWER 34 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1990:586059 HCAPLUS

DOCUMENT NUMBER:

113:186059

TITLE:

Recombinant manufacture of fusion protein of human

T-cell leukemia virus 1 (HTLV-I) and human

immunodeficiency virus (HIV) envelope proteins

INVENTOR(S):

Longiaru, Mathew; Scherer, Bradley John; Terry, Robert

William

PATENT ASSIGNEE(S):

Hoffmann-La Roche, F., und Co. A.-G., Switz.

SOURCE:

Eur. Pat. Appl., 25 pp. CODEN: EPXXDW

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	ENT NO.		KIND	DATE	APPLICATION NO.	DATE
	· 					
ΕP	345792		A2	19891213	EP 1989-110414	19890608
EΡ	345792	-	A3	19910502		
	R: AT,	BE,	CH, DE	, ES, FR,	GB, IT, LI, NL, SE	
DK	8902844		A	19891211	DK 1989-2844	19890609
ΑU	8936255		A1	19891214	AU 1989-36255	19890609
ΑU	627738		B2	19920903		
JP	02042987		A2	19900213	JP 1989-148228 .	19890609
RTTY	APPLN.	TNFO.	. :		US 1988-205401	19880610

The title fusion proteins comprising .gtoreq.1 epitope of HIV-1 envelope protein such as HIV-1 gp41, and .gtoreq.1 epitope of HTLV-I envelope protein are manufd. with recombinant cells. The fusion proteins may be used for the detection of antibodies to HIV and HTLV-I and HTLV-I-assocd. virus such as HTLV-II. Also given is a method for detecting the antibodies to the viruses using the fusion protein. Plasmid HIV-1 pENV(60)-HTLV-I-ENV-I contg. a chimeric gene encoding the N-terminal 60 amino acids of HIV-1 gp41 and 134 amino acids of HTLV-I envelope protein (amino acids 306-440) was constructed by std. procedures and transfected into Escherichia coli. The fusion protein was manufd. with the recombinant E. coli and purified by extn., solubilization, and chromatog. Immunoassay of the antibodies to HIV-1 virus in AIDS and AIDS-related

complex patients who were previously shown to be seropos. and of the antibodies in HTLV-I seropos. samples was given.

130003-41-7, Glycoprotein gp 160 (human immunodeficiency provirus 1 clone pH2Ex gene env protein moiety reduced)

RL: PRP (Properties)

(amino acid sequence of).

L12 ANSWER 35 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1990:135603 HCAPLUS

DOCUMENT NUMBER:

112:135603

TITLE:

ΙT

Solid phase immunoassay for an antibody and

recombinant proteins for use therein

INVENTOR(S):

Highfield, Peter Edmund; Duncan, Richard Julian

Stuart; Parker, David; Spence, Robert Paul

PATENT ASSIGNEE(S):

Wellcome Foundation Ltd., UK

SOURCE:

Eur. Pat. Appl., 30 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA.	TENT NO.		KIND	DATE	APPLICATION NO. DATE
EP	307149 307149 307149		A2 A3 B1	19890315 19890503 19930107	EP 1988-308170 19880902
	R: AT,	BE,		ES, FR,	GB, GR, IT, LI, LU, NL, SE
DK	8804908	-	À	19890305	DK 1988-4908 19880902
AU	8821825		A1	19890309	AU 1988-21825 19880902
AU	615670		В2	19911010	
JP	01163665		A2	19890627	JP 1988-220305 19880902
JP	2634203		B2	19970723	
ZA	8806555		Α	19900530	ZA 1988-6555 19880902
AT	84370		E	19930115	AT 1988-308170 19880902
ES	2051859		Т3	19940701	ES 1988-308170 19880902
AU	9182753		A1	19911121	AU 1991-82753 19910823
PRIORITY	APPLN.	INFO.	:		GB 1987-20800 19870904
					GB 1988-18030 19880728
					EP 1988-308170 19880902

AΒ An immunoassay for an antibody comprises: (i) contacting a solid phase, on which is immobilized a first recombinant peptide which presents an antigenic sequence to which the antibody is capable of binding, with a test sample; (ii) contacting the solid phase with a second recombinant peptide which presents the antigenic sequence, which is labeled and which was expressed in an organism of a different genus than that in which the first recombinant peptide was expressed; and (iii) detg. whether the test sample contained any antibody. A suitable protein for use in assaying for anti-p24 and anti-gp41 HIV-1 (human immunodeficiency virus 1) antibody is a fusion of a gag sequence comprising amino acids 121-356 and an env sequence comprising amino acids 542-674. The amino acids are numbered according to Meusing, et al. (1985). Plasmid pDM322 (prepn. described) contg. the region encoding amino acids 542-674 of the HIV-1 env gene was digested with EcoRI, filled in with Klenow fragment, digested with BamHI, and the 410-base-pair fragment was ligated to a SmaI/BamHI fragment of plasmid pDM614 (prepn. described) contg. the region of the HIV-1 gag gene encoding for amino acids 121-356. The ligated fragments were transformed into Escherichia coli TG1 and 1 recombinant plasmid, pDM624, was digested with EcoRI and BamHI to produce an 1120-base-pair fragment, which was transferred to plasmid pXY46X (prepn. described) to produce the expression plasmid pDM626. The env/gag fusion protein from pDM626 was purified and coated onto microtiter plate wells. Serum samples (50 .mu.L) were added to the wells, incubated for 30 min, and the wells were washed and treated

with 50 .mu.L peroxidase-conjugated antihuman Ig for 30 min. Upon addn. of enzyme substrate, antibodies to HIV-1 were detected by comparison to a std. All seroneg. samples tested neg., and all seropos. samples tested pos. (55/55 and 25/25, resp.). Construction of plasmids coding for foot-and-mouth disease virus VP1 protein-hepatitis B core antigen fusion products are also described.

IT 125857-53-6

RL: ANST (Analytical study)

(as env/gag fusion protein of human immunodeficiency virus 1, immunoassay for antibody in relation to)

IT 125857-38-7

RL: ANST (Analytical study)

(cloning and expression of, in Escherichia coli)

L12 ANSWER 36 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1988:623976 HCAPLUS

DOCUMENT NUMBER:

109:223976

TITLE:

Production of polypeptides derived from the envelope gene of human immunodeficiency virus in recombinant baculovirus-infected insect cells for use as vaccine

INVENTOR(S):

Cochran, Mark A.; Smith, Gale E.; Volvovitz, Franklin

PATENT ASSIGNEE(S):

Microgenesys, Inc., USA

SOURCE:

Eur. Pat. Appl., 26 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATE	NT NO.	•	KIND	DATE		API	PLICATION NO). I	DATE
	65785 65785		A2 A3	19880504 19891108		EP	1987-115085	; - ;	19871015
	R: AT,	BE, C	H, DE,	, ES, FR,	GB,	GR, I	IT, LI, LU,	NL,	SE
ZA 8	707752		A	19890628		ZA	1987-7752		19871015
DK 8	705419		A	19880417		DK	1987-5419		19871016
FI 8	704564		Α	19880417		FI	1987-4564		19871016
AU 8	779842		A1	19880421		AU	1987-79842	:	19871016
BR 8	705535		A	19880524		BR	1987-5535		19871016
HU 4	5095		A2	19880530		HU	1987-4666		19871016
JP 6	3207397		A2	19880826		JP	1987-262572	: :	19871016
CN 8	7107837		A	19881221		CN	1987-107837		19871016
DD 2	69629		A5	19890705		· DD	1987-308039) [19871016
DD 2	83935		A5	19901031		DD	1987-329440) :	19871016
DD 2	84046		A5	19901031		DD	1987-329441		19871016
PL 1	61165		В1	19930531		PL	1987-268266	; ;	19871016
PL 1	61448		В1	19930630	•	\mathtt{PL}	1987-293520) :	19871016
AU 9	188324		A1	19920430		ΑU	1991-88324	-	19911129
LV 1	0654		В	19951020		LV	1993-344	:	19930514
LV 1	0495		В	19951020	-	LV	1993-345	-	19930514
LV 1	0496		В	19951020		LV	1993-346	-	19930514
PRIORITY .	APPLN. I	NFO.:			Ţ	JS 198	86-920197		19861016

AB AIDS virus antigenic proteins are produced using a recombinant insect virus. Recombinant plasmids were constructed by inserting into plasmids MGS-3, -4, or -5 the cDNA for the HIV full-length envelope gp160 glycoprotein (or a fragment thereof from plasmid NA-2). In some of the recombinant plasmids, the viral glycoprotein cDNA was fused with the gene for hepatitis B surface antigen or interleukin 2 signal peptide. The recombinant plasmids were calcium phosphate-pptd. with Autographa californica nuclear polyhedrosis virus and added to Spodoptera furgiperda cells. Cells harboring recombinant viruses contg. inserts of HIV env sequences were isolated, which produced the desired viral proteins.

IT 117537-38-9, 1-757-Glycoprotein gp 160 (human immunodeficiency

provirus clone NA-2 gene env protein moiety reduced) 117537-39-0, 472-757-Glycoprotein gp 160 (human immunodeficiency provirus clone NA-2 gene env protein moiety reduced) 117537-39-0D, 472-757-Glycoprotein gp 160 (human immunodeficiency provirus clone NA-2 gene env protein moiety reduced), fusion products with interleukin 2 signal peptide 117537-40-3, 472-861-Glycoprotein gp 160 (human immunodeficiency provirus clone NA-2 gene env protein moiety reduced) 117537-41-4D, 473-861-Glycoprotein gp 160 (human immunodeficiency provirus clone NA-2 gene env protein moiety reduced), fusion products with interleukin 2 signal peptide RL: PRP (Properties)

(amino acid sequence of and expression in insect cells of cDNA for) 117537-33-4, Glycoprotein gp 160 (human immunodeficiency provirus clone NA-2 gene env protein moiety reduced)

RL: PRP (Properties)

(expression in insect cells of cDNA for)

L12 ANSWER 37 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1988:210167 HCAPLUS

DOCUMENT NUMBER:

108:210167

TITLE:

ΙT

Construction of recombinant vaccinia and baculovirus

producing antigenic proteins for use as vaccines for

INVENTOR(S):

Hu, Shiu Lok; Purchio, Anthony; Madisen, Linda

PATENT ASSIGNEE(S):

Oncogen, USA Belg., 158 pp.

SOURCE:

CODEN: BEXXAL

DOCUMENT TYPE:

Patent French

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE		APPLICATION NO.	DATE
BE 905492	A1	19870325		BE 1986-217210	19860925
ZA 8607281	A	19870527		ZA 1986-7281	19860924
DE 3690508	T	19880623		DE 1986-3690508	19860925
US 5081029	. A	19920114		US 1989-304926	19890201
PRIORITY APPLN.	INFO.:		US	1985-779909	19850925
			US	1986-842984	19860327
			US	1986-905217	19860909
•			US	1986-909447	19860919
			WO	1986-US2002	19860925

Recombinant nonpathogenic viruses (e.g. vaccinia, baculovirus) producing AΒ lymphadenopathy assocd. virus/human T-cell leukemia virus type III (LAV/HTLVIII) antigenic proteins are constructed which can be used as vaccines against AIDS. Vectors were constructed contg. the LAV/HTLVIII env or gag gene or gene fragment under the control of the vaccinia $7.5~{\rm K}$ promoter or the Autographa californica polyhedrin gene promoter. vectors were used to produce recombinant vaccinia or Autographacalifornica viruses by homologous recombination. The resultant recombinant viruses showed immunogenic activity in mice and chimpanzee. Virus v-env5 (producing env protein) stimulated interleukin 2 prodn. by T-cells.

TΤ 95568-30-2

RL: BIOL (Biological study)

(cloning of gene for, in recombinant virus vaccine construction)

L12 ANSWER 38 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:

1987:616034 HCAPLUS

DOCUMENT NUMBER:

107:216034

TITLE: Polypeptides mimicking antigenic determinants of human

T-cell lymphotropic virus type III (HTLV-III), their production by recombinant DNA techniques and their use

in immunoassays and vaccines

INVENTOR(S): Berman, Michael L.; Crush, Sylvia A.; Wong-Staal,

Flossie; Gallo, Robert C.

PATENT ASSIGNEE(S): AKZO N. V., Neth.

SOURCE: Eur. Pat. Appl., 33 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO. DATE	
	A2 A3	19870701 19890712	2	
EP 227169	B1	19930317		
R: AT, BE, AT 87103		, ES, FR, 19930415	GB, GR, IT, LI, LU, NL, SE AT 1986-202213 19861208	
ES 2054616	тз E	19930415		
AU 8666519	A1	19870702		
AU 612315	B2	19910711		
FI 8605123	A	19870618		
FI 91282	В	19940228	3	
FI 91282	С	19940610		
NO-8605094	А	19870618	NO 1986-5094 19861216	
NO 171477	В	19921207		
NO 171477	С	19930317		
JP 62240863	A2	19871021		
JP 2587414	B2	19970305		
DK 8606107	A	19870618		
PRIORITY APPLN. INFO	. :		US 1985-809872 19851217	
			US 1986-861900 19860508	
			US 1986-887294 19860718	
			US 1986-927577 19861114 EP 1986-202213 19861208	
70 7 '			EP 1986-202213 19861208	

AB An immunochem. reagent comprising a combination of .gtoreq.2 synthetic polypeptide sequences mimicking .gtoreq.1 antigenic determinant of the gag antigen, glycoprotein gp120, and glycoprotein gp41 of HTLV-III is prepd. by recombinant DNA techniques for use in immunoassays and vaccines. Fragments of a genomic clone (.lambda.HAT-3) of an HTLV-III prophage in bacteriophage were used in construction of cloning vectors derived from pBR322 for cloning and expression of the appropriate immunogenic polypeptide genes in Escherichia coli. The polypeptides were recovered from harvested cells and used for ELISA of test serums for HTLV-III antibody.

IT 111274-36-3P 111274-47-6P

RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)

(manuf. of, with recombinant Escherichia coli for immunoassays and vaccines for human T-cell lymphotropic virus type III)

L12 ANSWER 39 OF 39 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1987:493086 HCAPLUS

DOCUMENT NUMBER: 107:93086

TITLE: Recombinant acquired immune deficiency syndrome (AIDS)

viral envelope protein and method of testing for AIDS Crowl, Robert Mitchell; Gallo, Robert Charles; Reddy,

INVENTOR(S): Crowl, Robert Mitchell; Gallo, Robert Charles; F

Eragam Premkumar; Shaw, George Mead; Wong-Staal,

Flossie Yeeching

PATENT ASSIGNEE(S): Hoffmann-La Roche, F., und Co. A.-G., Switz.; United

States Dept. of Health and Human Services

Eur. Pat. Appl., 46 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

SOURCE:

Patent English

LANGUAGE: FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE		APPLICATION NO.	DATE
EP 199301 EP 199301 EP 199301	A1 B1 B2	19861029 19931229 19970709		EP 1986-105371	19860418
R: AT,			TT.	I.T. NI. SE	
US 725021	A0	19880601	,	US 1985-725021	19850419
DK 8601772		19861020		US 1985-725021 DK 1986-1772	19860417
		19960617			
FI 8601626	A	19861020		FI 1986-1626	19860417
NO 8601546	A	19861020		NO 1986-1546	
	A1	19861023			19860418
	B2	19900405			
JP 62012799	A2	19870121		JP 1986-89830	19860418
	A1	19870601		ES 1986-554155	19860418
AT 99330	E	19940115			19860418
ES 557293	A1	19880301		ES 1987-557293	19870112
ES 557293	, A5	19880328			
ES 557294	A1	19880301		ES 1987-557294	19870112
ES 557294	A5 .	19880328		•	
	A1	19880301		ES 1987-557295	19870112
ES 557295	A5	19880328			
	A1	19880301		ES 1987-557296	19870112
	A5	19880328			
US 6077935		20000620		US 1991-811896	19911220
US 5773210	A	19980630		US 1993-132406	19931006
US 5869233	A	19990209		US 1995-456352	19950601
PRIORITY APPLN. I	NFO.:			S 1985-725021 A	
				SP 1986-105371 A	
			U	IS 1988-244590 B IS 1991-811896 A	1 19880913
•					
			Ü	IS 1993-132406 A	3 19931006

The AIDS viral envelope protein was prepd. by recombinant DNA techniques AΒ for use as an antigen in detection of AIDS virus antibodies in human blood, in prodn. of antibodies for detection of the viral antigen, and as a vaccine in immunization against AIDS virus. Use of this pure antigen overcomes problems of nonspecificity assocd. with the virus-contg. human cell exts. used previously. The envelope protein has a mol. wt. of 97,200 and has 32 potential N-glycosylation sites; its amino acid sequence and corresponding nucleotide sequence are presented. The protein has a hydrophobic region at the middle which includes a processing site for cleavage of the precursor protein into exterior and transmembrane proteins. Another short hydrophobic region near the N-terminus may constitute a signal sequence. Comparison of the amino acid sequences of envelope proteins from lymphadenopathy-assocd. virus, AIDS-assocd. retrovirus 2, and 3 isolates of human T-cell leukemia virus III (HTLV-III) revealed 1-20% divergence among the sequences, suggesting that these are all variants of the same AIDS virus. For example, the cloned proviral genome of HTLV-III was digested with EcoRI and HindIII and a 2400-bp fragment was inserted into a pBR322 deriv. for cloning and expression in Escherichia coli.

IT 98615-73-7

RL: ANST (Analytical study)
(envelope protein of AIDS virus in relation to)

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E1 THROUGH E31 ASSIGNED
=> fil reg
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STRUCTURE FILE UPDATES: 19 MAY 2003 HIGHEST RN 518003-32-2
DICTIONARY FILE UPDATES: 19 MAY 2003 HIGHEST RN 518003-32-2
TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003
 Please note that search-term pricing does apply when
 conducting SmartSELECT searches.
Crossover limits have been increased. See HELP CROSSOVER for details.
Experimental and calculated property data are now available. See HELP
PROPERTIES for more information. See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf
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L13
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L13 ANSWER 1 OF 31 REGISTRY COPYRIGHT 2003 ACS
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    2: PN: JP2000333678 SEQID: 2 unclaimed sequence (9CI) (CA INDEX NAME)
CN
NTE
               ----- location ----- description
Aan-98
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SEQ
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651 LWNWFNITNW LWYIKLFIMI VGGLVGLRIV FAVLSIVNRV RQGYSPLSFQ

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L13
     ANSWER 2 OF 31 REGISTRY COPYRIGHT 2003 ACS
     264584-24-9 REGISTRY
RN
CN
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     extracellular domain) (9CI) (CA INDEX NAME)
SQL
     162
RN
     264584-24-9 REGISTRY
       101 ASWSNKSLEQ IWNNMTWMEW DREINNYTSL IHSLIEESQN QQEKNEQELL
SEO
                                      151 ELDKWASLWN WF
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REFERENCE
           1: 132:288345
    ANSWER 3 OF 31 REGISTRY COPYRIGHT 2003 ACS
     239445-66-0 REGISTRY
RN
CN
     Glycoprotein gp160 (human immunodeficiency virus 1 857-amino acid isoform)
     (9CI) (CA INDEX NAME)
OTHER NAMES:
CN
     1: PN: BR9710824 SEQID: 1 claimed protein
SOL
    857
RN
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                                                   __ _____
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REFERENCE
           1: 135:191275
REFERENCE
           2: 131:180832
L13 ANSWER 4 OF 31 REGISTRY COPYRIGHT 2003 ACS
RN 
     235787-61-8 REGISTRY
CN
     L-Phenylalanine, L-tyrosyl-L-threonyl-L-seryl-L-leucyl-L-isoleucyl-L-
     histidyl-L-seryl-L-leucyl-L-isoleucyl-L-.alpha.-glutamyl-L-.alpha.-
     glutamyl-L-seryl-L-glutaminyl-L-asparaginyl-L-glutaminyl-L-glutaminyl-L-
     .alpha.-glutamyl-L-lysyl-L-asparaginyl-L-.alpha.-glutamyl-L-glutaminyl-L-
     .alpha.-qlutamyl-L-leucyl-L-leucyl-L-.alpha.-qlutamyl-L-leucyl-L-.alpha.-
     aspartyl-L-lysyl-L-tryptophyl-L-alanyl-L-seryl-L-leucyl-L-tryptophyl-L-
     asparaginyl-L-tryptophyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN
     118: PN: WO0069900 SEQID: 1419 unclaimed protein
CN
     1: PN: US6017536 SEQID: 1 claimed protein
CN
     1: PN: WO0143779 SEQID: 1 claimed protein
     1: PN: WO0151673 TABLE: 5 unclaimed protein
CN
CN
     1: PN: WO0164013 SEQID: 15 claimed protein
CN
     1: PN: WO0170262 SEQID: 1 claimed protein
     2: PN: WO0159457 SEQID: 5 unclaimed protein
CN
     34: PN: WO0066622 SEQID: 34 claimed protein
CN
     485: PN: WOO103723 TABLE: 2 unclaimed protein
CN
     5: PN: WO0040616 SEQID: 5 claimed protein
CN
     9: PN: WO0164710 SEQID: 10 unclaimed protein
CN
    36
```

SQL RN

235787-61-8 REGISTRY

SEQ 1 YTSLIHSLIE ESQNQQEKNE QELLELDKWA SLWNWF

HITS AT: 1-36

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 135:317171

REFERENCE 2: 135:287512

REFERENCE 3: 135:236401

REFERENCE 4: 135:236400

REFERENCE 5: 135:190383

REFERENCE 6: 135:136407

REFERENCE 7: 135:60176

REFERENCE 8: 134:125927

REFERENCE 9: 134:21425

REFERENCE 10: 133:349157

L13 ANSWER 5 OF 31 REGISTRY COPYRIGHT 2003 ACS

RN **178038-95-4** REGISTRY

CN Antigen (synthetic DEV-1 anti-human antibody) (9CI) (CA INDEX NAME)

NTE

type	location		description
uncommon	Aaa-47	-	-
uncommon	Aaa-48	_	-
uncommon	Aaa-49	-	-
uncommon	Aaa-50		- ·
uncommon	Aaa-51	-	-
uncommon	Aaa-52	-	-
uncommon	Aaa-53		-
uncommon	Aaa-54	-	-
uncommon	Aaa-55	-	-
uncommon	Aaa-56	-	-
uncommon	Aaa-57		ta aar variatii aa ka
uncommon	Aaa-58	-	-
uncommon	Aaa-59	-	-
uncommon	Aaa-60	-	-
uncommon	Aaa-61	-	-
uncommon	Aaa-62	-	-
uncommon	Aaa-63	-	-
uncommon	Aaa-64	-	-
uncommon	Aaa-65	-	-
uncommon	Aaa-66	-	_
uncommon	Aaa-67	-	-
uncommon	Aaa-68	-	-
uncommon	Aaa-69	-	-
uncommon	Aaa-70	-	-
uncommon	Aaa-210	-	-
uncommon	Aaa-211	-	-
uncommon	Aaa-212	-	-
uncommon	Aaa-213	-	-
uncommon	Aaa-214	-	-
uncommon	Aaa-215	-	-

```
Parkin 09 623533
               Aaa-216
uncommon
               Aaa-217
uncommon
               Aaa-218
uncommon
               Aaa-219
uncommon
               Aaa-220
uncommon
uncommon
               Aaa-221
               Aaa-222
uncommon
uncommon
               Aaa-223
               Aaa-224
uncommon
uncommon
               Aaa-225
               Aaa-226
uncommon
uncommon
               Aaa-227
               Aaa-228<sup>.</sup>
uncommon
               Aaa-229
uncommon
               Aaa-230
uncommon
               Aaa-231
uncommon
uncommon
               Aaa-232
uncommon
               Aaa-233
uncommon
               Aaa-234
_____
SOL 282
RN
    178038-95-4 REGISTRY
SEO
      151 QIWNNMTWME WDREINNYTS LIHSLIEESQ NQQEKNEQEL LELDKWASLW
                           201 NWFNITNWLX XXXXXXXXXX XXXXXXXXX XXXXVNRVRO GYSPLSFOTH
HITS AT:
          168-203
REFERENCE
         1: 125:50774
```

L13 ANSWER 6 OF 31 REGISTRY COPYRIGHT 2003 ACS

RN **171886-27-4** REGISTRY

CN Glycoprotein (human immunodeficiency virus 1 strain NL4-3 clone pNOTA/NL4-3/4.20 gene env) (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

Glycoprotein (human immunodeficiency provirus 1 strain NL4-3 clone pNOTA/NL4-3/4.20 gene env)

OTHER NAMES:

CN GenBank U26942-derived protein

SQL 854

171886-27-4 REGISTRY RN

SEQ 601 ICTTAVPWNA SWSNKSLEQI WNNMTWMEWD REINNYTSLI HSLIEESQNQ

651 OEKNEOELLE LDKWASLWNW FNITNWLWYI KLFIMIVGGL VGLRIVFAVL

HITS AT: 636-671

REFERENCE 1: 124:46731

L13 ANSWER 7 OF 31 REGISTRY COPYRIGHT 2003 ACS

169874-95-7 REGISTRY RN

Glycoprotein gp 41 (human immunodeficiency virus 1 strain NL4-3 C-terminal CN fragment) (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

Glycoprotein gp 41 (human immunodeficiency provirus 1 strain NL4-3 C-terminal fragment)

OTHER NAMES:

17: PN: US6015661 SEQID: 641 claimed protein CN

640: PN: US6010895 SEQID: 641 unclaimed protein CN

SQL 237

169874-95-7 REGISTRY RN

SEQ 1 EQIWNNMTWM EWDREINNYT SLIHSLIEES QNQQEKNEQE LLELDKWASL 51 WNWFNITNWL WYIKLFIMIV GGLVGLRIVF AVLSIVNRVR QGYSPLSFQT HITS AT: 19-54 REFERENCE 1: 132:118353 REFERENCE 2: 132:74538 REFERENCE 3: 123:310209 L13 ANSWER 8 OF 31 REGISTRY COPYRIGHT 2003 ACS 165308-52-1 REGISTRY RN CN Protein (human immunodeficiency virus 1 gene env) (9CI) (CA INDEX NAME) SQL 519 RN **165308-52-1** REGISTRY SEQ 401 TTAVPWNASW SNKSLEQIWN HTTWMEWDRE INNYTSLIHS LIEESQNQQE _____ 451 KNEQELLELD KWASLWNWFN ITNWLWYIKL FIMIVGGLVG LRIVFAVLSI ______ HITS AT: 434-469 REFERENCE 1: 123:76420 ANSWER 9 OF 31 REGISTRY COPYRIGHT 2003 ACS L13 RN **162995-84-8** REGISTRY 517-750-Glycoprotein gp 41env (human immunodeficiency virus 1 gene env) CN (9CI) (CA INDEX NAME) SOL 235 RN 162995-84-8 REGISTRY 101 ASWSNKSLEQ IWNNMTWMEW DREINNYTSL IHSLIEESQN QQEKNEQELL SEQ ____ ______ 151 ELDKWASLWN WFNITNWLWY IKIFIMIVGG LVGLRIVFAV LSIVNRVRQG HITS AT: 127-162 REFERENCE 1: 122:281521 L13 ANSWER 10 OF 31 REGISTRY COPYRIGHT 2003 ACS RN 162995-83-7 REGISTRY (478-522)-(548-679)-(705-757)-Glycoprotein gp 41env (human)immunodeficiency virus 1 gene env) (9CI) (CA INDEX NAME) SOL 222 162995-83-7 REGISTRY RN SEO 101 SGKLICTTAW PWNASWSNKS LEQIWNNNMT WMEWDREINN YTSLIHSLIE 151 ESQNQQEKNE QELLELDKWA SLWNWFAVLS IVNRVRQGYS PLSFQTHLPT _____ ____ HITS AT: 141-176 REFERENCE 1: 122:281521 ANSWER 11 OF 31 REGISTRY COPYRIGHT 2003 ACS 1.13159519-65-0 REGISTRY RN CN L-Phenylalaninamide, N-acetyl-L-tyrosyl-L-threonyl-L-seryl-L-leucyl-Lisoleucyl-L-histidyl-L-seryl-L-leucyl-L-isoleucyl-L-.alpha.-glutamyl-L-.alpha.-qlutamyl-L-seryl-L-qlutaminyl-L-asparaqinyl-L-glutaminyl-Lglutaminyl-L-.alpha.-glutamyl-L-lysyl-L-asparaginyl-L-.alpha.-glutamyl-L-

```
glutaminyl-L-.alpha.-glutamyl-L-leucyl-L-leucyl-L-.alpha.-glutamyl-L-
    leucyl-L-.alpha.-aspartyl-L-lysyl-L-tryptophyl-L-alanyl-L-seryl-L-leucyl-L-
     tryptophyl-L-asparaginyl-L-tryptophyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN
    1: PN: US20020146415 PAGE: 10 claimed protein
    1: PN: US20030044411 PAGE: 10 claimed protein
CN
    1: PN: WO0155439 SEQID: 1 claimed protein
CN
    1: PN: WO0224149 PAGE: 24 claimed protein
CN
    414: PN: WO0164013 FIGURE: 24 claimed protein
CN
CN
    636: PN: WO0151673 FIG: 54 claimed protein
CN
    DP 178
CN
    Enfuvirtide
CN
    Pentafuside
    T 20
CN
CN T 20 (peptide)
NTE modified
type
               ----- location ----- description
terminal mod. Tyr-1 - N-acetyl terminal mod. Phe-36 - C-terminal amide
______
SQL 36
RN
    159519-65-0 REGISTRY
SEO
        1 YTSLIHSLIE ESQNQQEKNE QELLELDKWA SLWNWF
          HITS AT:
          1 - 36
**RELATED SEQUENCES AVAILABLE WITH SEQLINK**
         1: 138:297119
REFERENCE
REFERENCE
           2: 138:247786
REFERENCE
           3: 138:238191
           4: 138:218034
REFERENCE
REFERENCE
           5: 138:215262
REFERENCE
           6: 138:180054
REFERENCE
           7: 138:131079
REFERENCE
           8: 138:130638
REFERENCE
           9: 138:121507
REFERENCE 10: 138:19459
L13 ANSWER 12 OF 31 REGISTRY COPYRIGHT 2003 ACS
    158130-91-7 REGISTRY
RN
    1-198-Glycoprotein gp 41 (human immunodeficiency virus 1 clone HXB2R3 gene
    env) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
    1-198-Glycoprotein gp 41 (human immunodeficiency provirus 1 clone HXB2R3
    gene env)
   198
SQL
    158130-91-7 REGISTRY
RN
SEQ
      101 ASWSNKSLEQ IWNHTTWMEW DREINNYTSL IHSLIEESQN QQEKNEQELL
```

151 ELDKWASLWN WFNITNWLWY IKLFIMIVGG LVGLRIVFAV LSIVNRVR

HITS AT: 127-162

REFERENCE 1: 121:195914

T.13 ANSWER 13 OF 31 REGISTRY COPYRIGHT 2003 ACS

158130-90-6 REGISTRY RN

CN 1-252-Glycoprotein qp 41 (human immunodeficiency virus 1 clone HXB2R3 gene env) (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

1-252-Glycoprotein gp 41 (human immunodeficiency provirus 1 clone HXB2R3 gene env) .

SQL 241

RN 158130-90-6 REGISTRY

SEQ 101 ASWSNKSLEQ IWNHTTWMEW DREINNYTSL IHSLIEESQN QQEKNEQELL

151 ELDKWASLWN WFNITNWLWY IKLFIMIVGG LVGLRIVFAV LSIVNRVRQG

HITS AT: 127-162

REFERENCE 1: 121:195914

ANSWER 14 OF 31 REGISTRY COPYRIGHT 2003 ACS L13

158130-89-3 REGISTRY RN

CN 1-264-Glycoprotein gp 41 (human immunodeficiency virus 1 clone HXB2R3 gene env) (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

1-264-Glycoprotein qp 41 (human immunodeficiency provirus 1 clone HXB2R3 gene env)

SQL 264

RN. **158130-89-3** REGISTRY

SEQ 101 ASWSNKSLEQ IWNHTTWMEW DREINNYTSL IHSLIEESQN QQEKNEQELL

____ _______

151 ELDKWASLWN WFNITNWLWY IKLFIMIVGG LVGLRIVFAV LSIVNRVRQG

HITS AT: 127-162

REFERENCE 1: 121:195914

L13 ANSWER 15 OF 31 REGISTRY COPYRIGHT 2003 ACS

RN **158130-88-2** REGISTRY

1-284-Glycoprotein gp 41 (human immunodeficiency virus 1 clone HXB2R3 gene env) (9CI) (CA INDEX ŇAME)

OTHER CA INDEX NAMES:

1-284-Glycoprotein gp 41 (human immunodeficiency provirus 1 clone HXB2R3 gene env)

SQL 284

RN 158130-88-2 REGISTRY

SEQ 101 ASWSNKSLEQ IWNHTTWMEW DREINNYTSL IHSLIEESQN QQEKNEQELL

151 ELDKWASLWN WFNITNWLWY IKLFIMIVGG LVGLRIVFAV LSIVNRVRQG

HITS AT: 127-162

REFERENCE 1: 121:195914

ANSWER 16 OF 31 REGISTRY COPYRIGHT 2003 ACS L13

RN **158130-87-1** REGISTRY

1-302-Glycoprotein gp 41 (human immunodeficiency virus 1 clone HXB2R3 gene CN

env) (9CI) (CA INDEX NAME) OTHER CA INDEX NAMES: 1-302-Glycoprotein gp 41 (human immunodeficiency provirus 1 clone HXB2R3 SQL 302 158130-87-1 REGISTRY RN SEO 101 ASWSNKSLEQ IWNHTTWMEW DREINNYTSL IHSLIEESQN QQEKNEQELL ---- ------- -------151 ELDKWASLWN WFNITNWLWY IKLFIMIVGG LVGLRIVFAV LSIVNRVRQG ======== == HITS AT: 127-162 REFERENCE 1: 121:195914 L13 ANSWER 17 OF 31 REGISTRY COPYRIGHT 2003 ACS **158130-86-0** REGISTRY RN CN 1-332-Glycoprotein gp 41 (human immunodeficiency virus 1 clone HXB2R3 gene env) (9CI) (CA INDEX NAME) OTHER CA INDEX NAMES: 1-332-Glycoprotein gp 41 (human immunodeficiency provirus 1 clone HXB2R3 gene env) SQL 332 RN **158130-86-0** REGISTRY SEO 101 ASWSNKSLEQ IWNHTTWMEW DREINNYTSL IHSLIEESQN QQEKNEQELL 151 ELDKWASLWN WFNITNWLWY IKLFIMIVGG LVGLRIVFAV LSIVNRVRQG HITS AT: 127-162 REFERENCE 1: 121:195914 L13 ANSWER 18 OF 31 REGISTRY COPYRIGHT 2003 ACS RN **158130-85-9** REGISTRY Glycoprotein gp 41 (human immunodeficiency virus 1 clone HXB2R3 gene env) (9CI) (CA INDEX NAME) OTHER CA INDEX NAMES: Glycoprotein gp 41 (human immunodeficiency provirus 1 clone HXB2R3 gene OTHER NAMES: 5: PN: US6294341 SEQID: 7 unclaimed protein SQL RN **158130-85-9** REGISTRY 101 ASWSNKSLEQ IWNHTTWMEW DREINNYTSL IHSLIEESQN QQEKNEQELL SEQ 151 ELDKWASLWN WFNITNWLWY IKLFIMIVGG LVGLRIVFAV LSIVNRVRQG HITS AT: 127-162 1: 135:267203 REFERENCE 2: 121:195914 REFERENCE L13 ANSWER 19 OF 31 REGISTRY COPYRIGHT 2003 ACS **144903-86-6** REGISTRY RN Glycoprotein (human immunodeficiency virus 1 clone pHXB2gpt gene env CN precursor protein moiety reduced) (9CI) (CA INDEX NAME) OTHER CA INDEX NAMES:

Glycoprotein (human immunodeficiency provirus 1 clone pHXB2gpt gene env precursor protein moiety reduced) SQL 856

RN **144903-86-6** REGISTRY

SEQ 601 GKLICTTAVP WNASWSNKSL EQIWNHTTWM EWDREINNYT SLIHSLIEES

-- -------

651 QNQQEKNEQE LLELDKWASL WNWFNITNWL WYIKLFIMIV GGLVGLRIVF

HITS AT: 639-674

REFERENCE 1: 118:3468

L13 ANSWER 20 OF 31 REGISTRY COPYRIGHT 2003 ACS

RN 130003-41-7 REGISTRY

CN Glycoprotein gp 160 (human immunodeficiency virus 1 clone pH2Ex gene env protein moiety reduced) (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Glycoprotein gp 160 (human immunodeficiency provirus 1 clone pH2Ex gene env protein moiety reduced)

SQL 856

RN 130003-41-7 REGISTRY

SEQ 601 KLICTTAVPW NASWSNKLGS QIWNHTTWME WDREINNYTS LIHSLIEESQ

=== ========

651 NQQEKNEQEL LELDKWASLW NWFNITNWLW YIKLFIMIVG GLVGLRIVFA

HITS AT: 638-673

REFERENCE 1: 113:186059

L13 ANSWER 21 OF 31 REGISTRY COPYRIGHT 2003 ACS

RN 125857-53-6 REGISTRY

CN Protein p 24 (human immunodeficiency virus 1 clone .lambda.HXB-3 reduced), N-(L-methionyl-L-seryl-L-prolyl-L-.alpha.-aspartyl-L-threonylglycyl-L-histidyl-L-seryl-L-seryl-L-glutaminyl-L-valyl-L-seryl-L-glutaminyl-L-asparaginyl-L-tyrosyl)-225-L-asparagine-226-L-serine-227-L-proline-, (227.fwdarw.41')-protein with 44-L-leucine-106-L-alanine-111-L-serine-116-L-lysine-119-L-glutamic acid-120-L-glutamine-123-L-glutamine-131-L-aspartic acid-135-L-asparagine-139-L-serine-142-L-histidine-143-L-serine-150-L-asparagine-174-glycine-175-L-aspartic acid-176-L-proline-41-176-glycoprotein gp 41 (human immunodeficiency virus 1 clone HIV-Zr6 gene env protein moiety reduced) (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Protein p 24 (human immunodeficiency provirus 1 clone .lambda.HXB-3 reduced), N-(L-methionyl-L-seryl-L-prolyl-L-.alpha.-aspartyl-L-threonylglycyl-L-histidyl-L-seryl-L-seryl-L-glutaminyl-L-valyl-L-seryl-L-glutaminyl-L-asparaginyl-L-tyrosyl)-225-L-asparagine-226-L-serine-227-L-proline-, (227.fwdarw.41')-protein with 44-L-leucine-106-L-alanine-111-L-serine-116-L-lysine-119-L-glutamic acid-120-L-glutamine-123-L-glutamine-131-L-aspartic acid-135-L-asparagine-139-L-serine-142-L-histidine-143-L-serine-150-L-asparagine-174-glycine-175-L-aspartic acid-176-L-proline-41-176-glycoprotein gp 41 (human immunodeficiency provirus 1 clone HIV-Zr6 gene env protein moiety reduced)

SQL 379

RN 125857-53-6 REGISTRY

SEQ 301 SGKLICTTAV PWNASWSNKS LEQIWNNMTW MEWDREINNY TSLIHSLIEE

= =======

351 SQNQQEKNEQ ELLELDKWAS LWNWFNGDP

HITS AT: 340-375

REFERENCE 1: 112:135603

L13 ANSWER 22 OF 31 REGISTRY COPYRIGHT 2003 ACS

RN 125857-38-7 REGISTRY

CN 37-176-Glycoprotein gp 41 (human immunodeficiency virus 1 clone HIV-Zr6 gene env protein moiety reduced), 37-L-methionine-38-L-asparagine-39-L-serine-40-L-proline-44-L-leucine-106-L-alanine-111-L-serine-116-L-lysine-119-L-glutamic acid-120-L-glutamine-123-L-glutamine-131-L-aspartic acid-135-L-asparagine-139-L-serine-142-L-histidine-143-L-serine-150-L-asparagine-174-glycine-175-L-aspartic acid-176-L-proline- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 37-176-Glycoprotein gp 41 (human immunodeficiency provirus 1 clone HIV-Zr6 gene env protein moiety reduced), 37-L-methionine-38-L-asparagine-39-L-serine-40-L-proline-44-L-leucine-106-L-alanine-111-L-serine-116-L-lysine-119-L-glutamic acid-120-L-glutamine-123-L-glutamine-131-L-aspartic acid-135-L-asparagine-139-L-serine-142-L-histidine-143-L-serine-150-L-asparagine-174-glycine-175-L-aspartic acid-176-L-proline-

SQL 140

RN 125857-38-7 REGISTRY

SEQ 101 YTSLIHSLIE ESQNQQEKNE QELLELDKWA SLWNWFNGDP

HITS AT: 101-136

REFERENCE 1: 112:135603

L13 ANSWER 23 OF 31 REGISTRY COPYRIGHT 2003 ACS

RN 117537-41-4 REGISTRY

CN 473-861-Glycoprotein gp 160 (human immunodeficiency virus clone NA-2 gene env protein moiety reduced) (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 473-861-Glycoprotein gp 160 (human immunodeficiency provirus clone NA-2 gene env protein moiety reduced)

SQL 389

RN **117537-41-4** REGISTRY

SEQ 151 SLEQIWNNMT WMEWDREINN YTSLIHSLIE ESQNQQEKNE QELLELDKWA

201 SLWNWFNITN WLWYIKIFIM IVGGLVGLRI VFAVLSIVNR VRQGYSPLSF

=====

HITS AT: 171-206

REFERENCE 1: 109:223976

L13 ANSWER 24 OF 31 REGISTRY COPYRIGHT 2003 ACS

RN 117537-40-3 REGISTRY

CN 472-861-Glycoprotein gp 160 (human immunodeficiency virus clone NA-2 gene env protein moiety reduced) (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 472-861-Glycoprotein gp 160 (human immunodeficiency provirus clone NA-2 gene env protein moiety reduced)

SQL 390

RN 117537-40-3 REGISTRY

SEQ 151 KSLEQIWNNM TWMEWDREIN NYTSLIHSLI EESQNQQEKN EQELLELDKW

201 ASLWNWFNIT NWLWYIKIFI MIVGGLVGLR IVFAVLSIVN RVRQGYSPLS

HITS AT: 172-207

REFERENCE 1: 109:223976

L13 ANSWER 25 OF 31 REGISTRY COPYRIGHT 2003 ACS

RN **117537-39-0** REGISTRY

CN 472-757-Glycoprotein gp 160 (human immunodeficiency virus clone NA-2 gene

Parkin 09 623533 env protein moiety reduced) (9CI) (CA INDEX NAME) OTHER CA INDEX NAMES: CN 472-757-Glycoprotein qp 160 (human immunodeficiency provirus clone NA-2 gene env protein moiety reduced) SQL 286 RN117537-39-0 REGISTRY SEQ 151 KSLEQIWNNM TWMEWDREIN NYTSLIHSLI EESQNQQEKN EQELLELDKW ______ 201 ASLWNWFNIT NWLWYIKIFI MIVGGLVGLR IVFAVLSIVN RVRQGYSPLS HITS AT: 172-207 1: 109:223976 REFERENCE L13 ANSWER 26 OF 31 REGISTRY COPYRIGHT 2003 ACS RN 117537-38-9 REGISTRY CN 1-757-Glycoprotein gp 160 (human immunodeficiency virus clone NA-2 gene env protein moiety reduced) (9CI) (CA INDEX NAME) OTHER CA INDEX NAMES: 1-757-Glycoprotein gp 160 (human immunodeficiency provirus clone NA-2 gene env protein moiety reduced) SOL 757 RN 117537-38-9 REGISTRY SEO 601 WGCSGKLICT TAVPWNASWS NKSLEQIWNN MTWMEWDREI NNYTSLIHSL 651 IEESQNQQEK NEQELLELDK WASLWNWFNI TNWLWYIKIF IMIVGGLVGL ___________________________________ HITS AT: 643-678 1: 109:223976 REFERENCE ANSWER 27 OF 31 REGISTRY COPYRIGHT 2003 ACS T.1.3 117537-33-4 REGISTRY RN CN Glycoprotein gp 160 (human immunodeficiency virus clone NA-2 gene env protein moiety reduced) (9CI) (CA INDEX NAME) OTHER CA INDEX NAMES: Glycoprotein gp 160 (human immunodeficiency provirus clone NA-2 gene env protein moiety reduced) SQL 850 RN117537-33-4 REGISTRY SEO 601 AVPWNASWSN KSLEQIWNNM TWMEWDREIN NYTSLIHSLI EESQNQQEKN 651 EOELLELDKW ASLWNWFNIT NWLWYIKIFI MIVGGLVGLR IVFAVLSIVN ------ -----HITS AT: 632 - 667REFERENCE 1: 109:223976 ANSWER 28 OF 31 REGISTRY COPYRIGHT 2003 ACS L13

RN 111274-47-6 REGISTRY

CN L-Lysine, L-.alpha.-glutamyl-L-isoleucyl-L-asparaginyl-L-asparaginyl-L-tyrosyl-L-threonyl-L-seryl-L-leucyl-L-isoleucyl-L-histidyl-L-seryl-L-leucyl-L-isoleucyl-L-alpha.-glutamyl-L-alpha.-glutamyl-L-alpha.-glutamyl-L-alpha.-glutamyl-L-lysyl-L-asparaginyl-L-alpha.-glutaminyl-L-alpha.-glutamyl-L-leucyl-L-alpha.-glutamyl-L-leucyl-L-alpha.-glutamyl-L-tryptophyl-L-alanyl-L-seryl-L-leucyl-L-tryptophyl-L-asparaginyl-L-tryptophyl-L-asparaginyl-L-tryptophyl-L-asparaginyl-L-asparaginyl-L-tryptophyl-L-threonyl-L-asparaginyl-L-tryptophyl-L-tryptophyl-L-isoleucyl-(9CI) (CA INDEX NAME)

```
Parkin 09 623533
SOL
     50
    111274-47-6 REGISTRY
RN
SEQ
        1 EINNYTSLIH SLIEESQNQQ EKNEQELLEL DKWASLWNWF NITNWLWYIK
              ------
HITS AT:
          5-40
REFERENCE
           1: 107:216034
    ANSWER 29 OF 31 REGISTRY COPYRIGHT 2003 ACS
T.13
    111274-36-3 REGISTRY
RN
CN
    L-Asparagine, L-.alpha.-glutamyl-L-isoleucyl-L-asparaginyl-L-asparaginyl-L-
     tyrosyl-L-threonyl-L-seryl-L-leucyl-L-isoleucyl-L-histidyl-L-seryl-L-
     leucyl-L-isoleucyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-seryl-L-
     glutaminyl-L-asparaginyl-L-glutaminyl-L-glutaminyl-L-.alpha.-glutamyl-L-
     lysyl-L-asparaginyl-L-.alpha.-glutamyl-L-glutaminyl-L-.alpha.-glutamyl-L-
     leucyl-L-leucyl-L-.alpha.-glutamyl-L-leucyl-L-.alpha.-aspartyl-L-lysyl-L-
     tryptophyl-L-alanyl-L-seryl-L-leucyl-L-tryptophyl-L-asparaginyl-L-
     tryptophyl-L-phenylalanyl- (9CI) (CA INDEX NAME)
SQL
RN
    111274-36-3 REGISTRY
SEQ
        1 EINNYTSLIH SLIEESQNQQ EKNEQELLEL DKWASLWNWF N
              HITS AT:
          5-40
          1: 107:216034
REFERENCE
    ANSWER 30 OF 31 REGISTRY COPYRIGHT 2003 ACS
L13
    98615-73-7 REGISTRY
RN
CN
    Glycoprotein (human immunodeficiency virus clone HXB-3 gene env protein
    moiety reduced) (9CI)
                         (CA INDEX NAME)
OTHER CA INDEX NAMES:
    Glycoprotein (human immunodeficiency provirus clone HXB-3 gene env protein
    moiety reduced)
OTHER NAMES:
    Glycoprotein (human T-cell leukemia provirus type III clone HXB-3 gene env
    'protein moiety reduced)
SQL
    856
RN
    98615-73-7 REGISTRY
      601 KLICTTAVPW NASWSNKSLE QIWNHTTWME WDREINNYTS LIHSLIEESQ
SEQ
                     ______
      651 NQQEKNEQEL LELDKWASLW NWFNITNWLW YIKLFIMIVG GLVGLRIVFA
          _____
HITS AT:
          638-673
REFERENCE
           1: 107:93086
REFERENCE
           2: 103:154983
L13 ANSWER 31 OF 31 REGISTRY COPYRIGHT 2003 ACS
RN
    95568-30-2 REGISTRY
CN
    Glycoprotein (human immunodeficiency virus clone .lambda.J19 gene env
```

protein moiety reduced) (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

Glycoprotein (human immunodeficiency provirus clone .lambda.J19 gene env protein moiety reduced)

OTHER NAMES:

CN Glycoprotein (lymphadenopathy-associated provirus clone .lambda.J19 gene env protein moiety reduced)

SQL 861

95568-30-2 REGISTRY RN

SEQ 601 WGCSGKLICT TAVPWNASWS NKSLEQIWNN MTWMEWDREI NNYTSLIHSL

=======

651 IEESQNQQEK NEQELLELDK WASLWNWFNI TNWLWYIKIF IMIVGGLVGL

HITS AT: 643-678

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 118:143346

REFERENCE 2: 108:210167

REFERENCE 3: 102:126416